



A VISUAL AID FOR THE
**Parent/Patient Information and
the Informed Consent Process**



Why is my child being invited to take part in the FIONA study?

Your child has:

★ CHRONIC KIDNEY DISEASE

- ☐ STAGE 1,
- ☐ STAGE 2,
- ☐ STAGE 3, OR
- ☐ SERUM CREATININE LEVEL ≤ 0.4 mg/dL IF YOUR CHILD IS LESS THAN 1 YEARS OLD.

AND

★ VERY HIGH URINE PROTEIN LEVELS

You are being asked to allow your child to take part in the FIONA study because your child has Chronic Kidney Disease (CKD) with very high urine protein levels. If you are a parent or legal guardian, the decision to allow your child to join this study is up to you.



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- ★ Introduce yourself and explain your role in the FIONA Study.
- ★ Explain that their child is invited to participate in the FIONA study because he/she has CKD with very high urine protein levels.
- ★ Explain that this is the beginning of the informed consent process, which will provide information to help parents decide whether this research study might be right for their child.
- ★ Show the participant the **current [IRB-approved or EC-approved] consent form**. Let them know that they should take time to read the consent form completely before making a decision about whether or not to participate - and that they will have the opportunity to ask any questions while reviewing this flip chart.
- ★ Encourage questions at any time.



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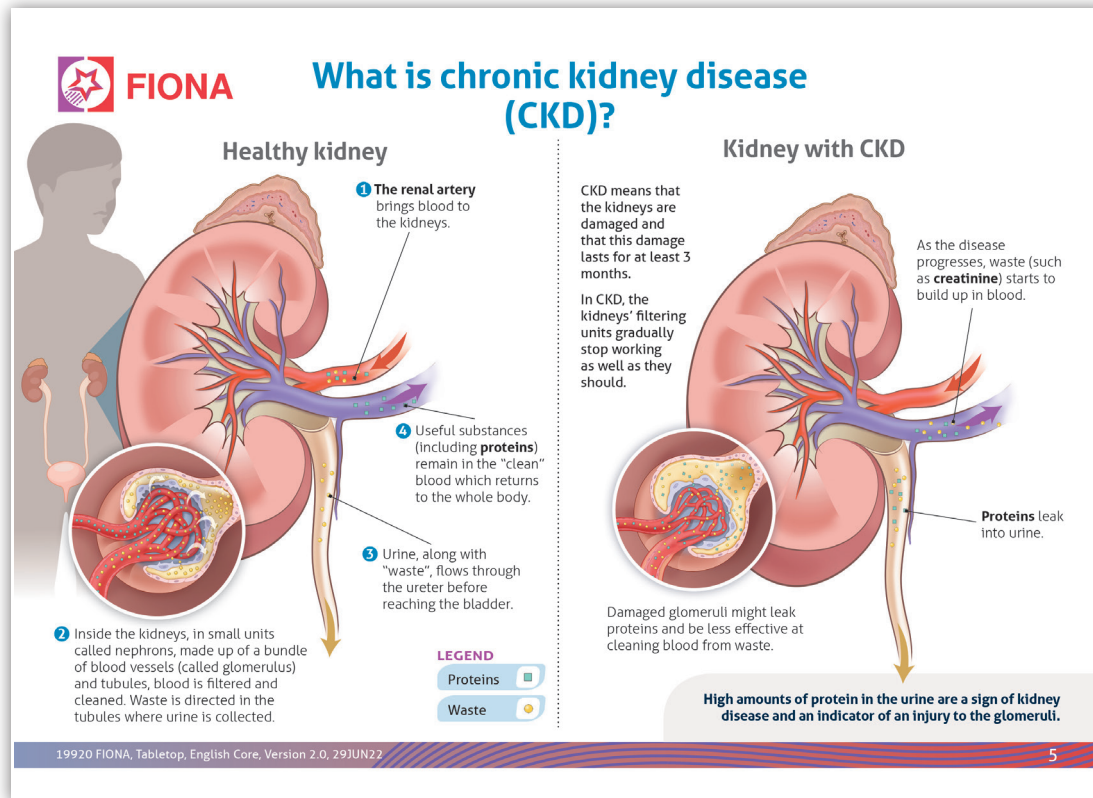
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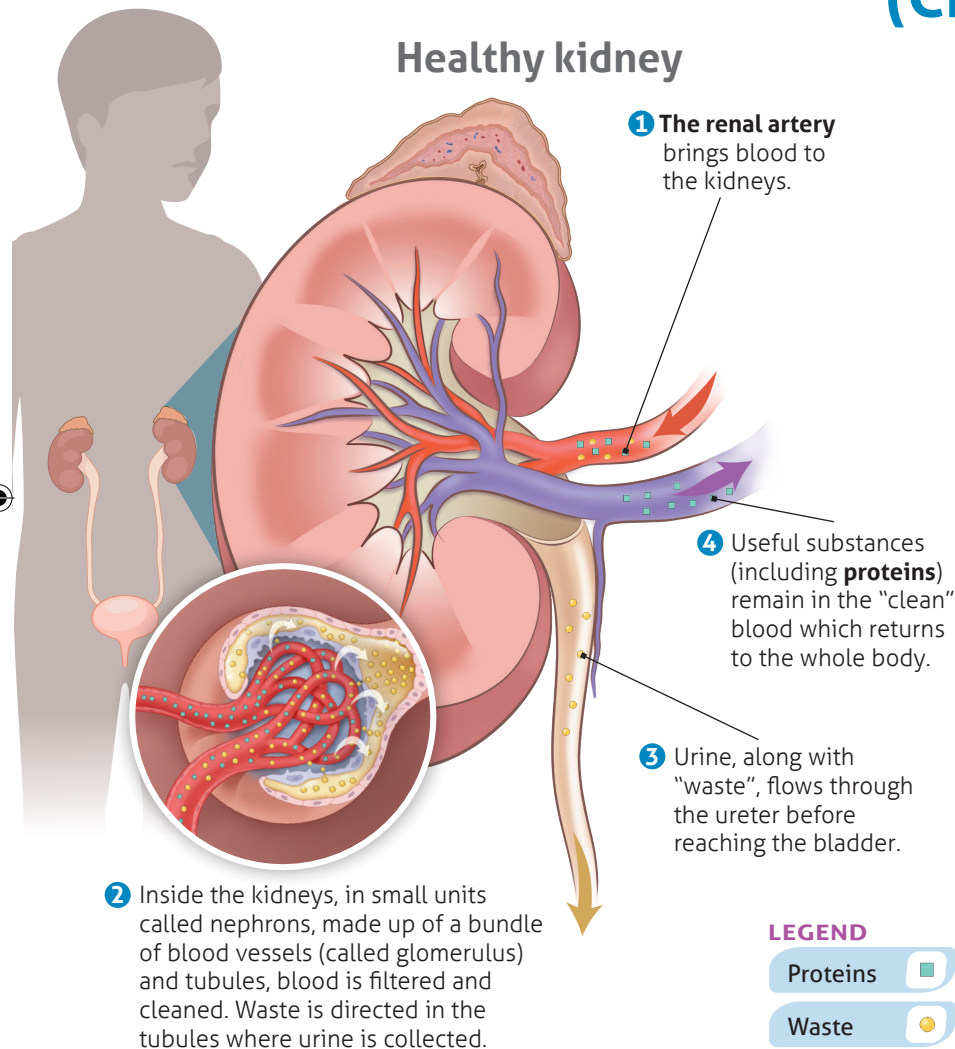
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- ✧ The illustrations may help parents and children understand what CKD is by comparing the **filtering function** in healthy kidney to the filtering function in CKD.
- ✧ This will help parents understand why blood and urine exams are needed.

What is chronic kidney disease (CKD)?

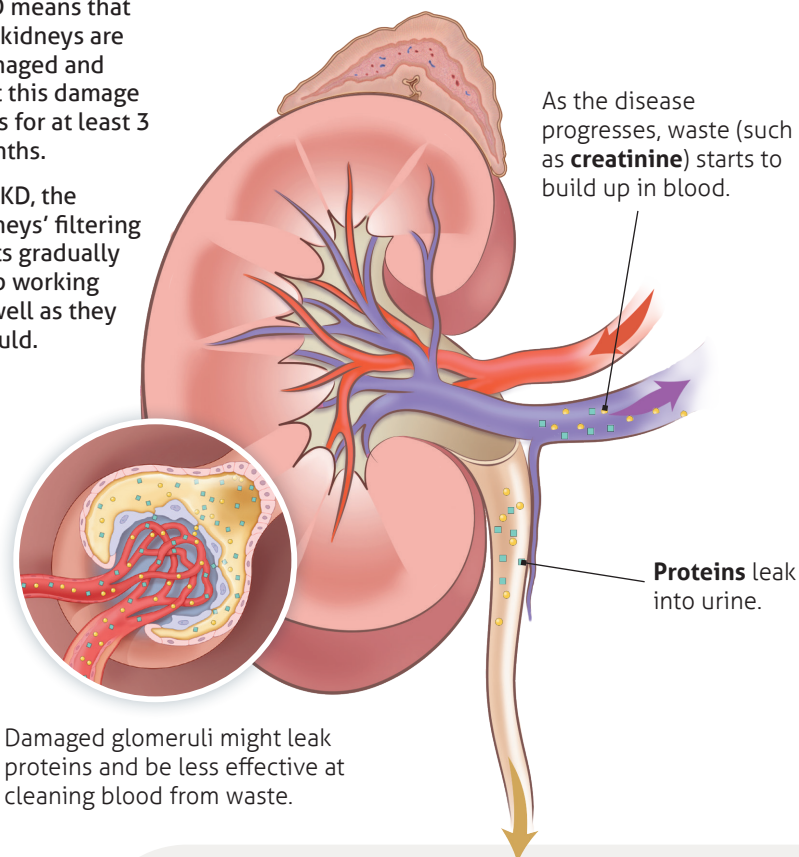
Healthy kidney



Kidney with CKD

CKD means that the kidneys are damaged and that this damage lasts for at least 3 months.

In CKD, the kidneys' filtering units gradually stop working as well as they should.



High amounts of protein in the urine are a sign of kidney disease and an indicator of an injury to the glomeruli.

CKD stages

CKD is defined as abnormalities of kidney structure or function, present for at least 3 months, with implications for health. There are 5 stages of CKD.

In stage 1, the kidneys' filtering function is still normal or even elevated. Structural anomalies or proteinuria might be present.

As the disease progresses, filtering units are damaged and the kidneys' filtering function starts decreasing.

The stages of CKD are defined on the basis of GFR. **GFR or glomerular filtration rate** is a number that tells how well kidneys are filtering blood. GFR is assessed based on how much creatinine (a waste) is found in the blood.

Stage	Kidney function	GFR (mL/min per 1.73m ²)
1	Normal or high	≥90
2	Mildly decreased	60-89
3	Moderately decreased	30-59
4	Severely decreased	15-29
5	Kidney failure	<15

Treatment

Treatment of CKD is aimed at slowing down the progression of CKD by controlling the risk factors that damage kidneys (e.g. high blood pressure, protein in urine and other risk factors).

- ☆ Explain which stage the child is in and what eGFR value (or creatinine value, if < 1 year of age) their child has.
- ☆ If known and if the parents or the child ask, take time to explain what causes CKD.
- ☆ Discuss that CKD is a progressive disease and that treatments can slow down its progression but may not stop it.
- ☆ Mention that CKD standard of care treatment will continue during the study.

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What is the purpose of the study?

The purpose of the FIONA study is to evaluate the safety and efficacy of a study drug compared to placebo, in children with CKD.

Study drug



This study drug is called finerenone. It is taken once a day as a tablet or as a suspension (liquid). It is an investigational drug in children. This means it can only be used in studies like this one in pediatric populations.

VS

Placebo



A placebo looks exactly like the study drug but does not have any active medicine in it. Using a placebo helps to learn whether the study drug works.

Your child will continue to receive standard of care for CKD. The study drug or placebo will be given in combination with the standard of care. In case your child has to stop taking some other medicine to take part in the study, the study doctor will discuss this with you in detail.

What will be evaluated?



EFFICACY: How well does the study drug work in children with CKD? This will be assessed by checking if the amounts of proteins in urine decrease.



SAFETY and TOLERABILITY: Is the study drug well tolerated and safe in children with CKD?



PHARMACOKINETICS (PK): How the drug moves into, through and out of the body.

- ✧ Explain the purpose of the study.
- ✧ Help parents understand what a placebo is and why it is used.
- ✧ Point out that you will not know if their child will be taking the study drug or placebo, but that you can find out in case of emergency.
- ✧ Reiterate that their child will continue standard of care treatment and that the study drug or placebo will be given together with their usual treatment.



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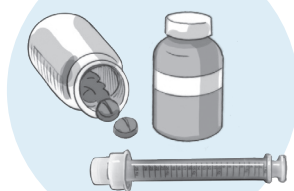
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What are the expected side effects?

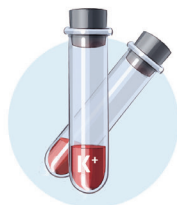
As with every investigational drug, you need to be aware that there may be side effects that are not known yet, and that your child may experience other side effects that have not been reported yet.

You will have to inform your study doctor in case your child experiences any new expected or unexpected symptoms.

Your child may experience some or none of these side effects.

10 or more adult patients, out of 100 taking the study drug in previous studies, experienced:

- ★ Increased potassium in the blood (hyperkalemia). Possible signs of high potassium levels in the blood may include feeling weak or tired, feeling sick to the stomach, numbness in the hands and lips, muscle cramps, irregular pulse rate.



1 to 10 adult patients, out of 100 taking the study drug in previous studies, experienced:

- ★ Low sodium levels in the blood (hyponatraemia). Possible signs may include feeling sick to the stomach, tiredness, headache, confusion, muscle weakness, spasms or cramps
- ★ Decrease in how well the kidneys filter blood (glomerular filtration rate decreased)
- ★ Low blood pressure (hypotension). Possible signs may include dizziness, lightheadedness, fainting.



Feeling weak or tired



Feeling sick to the stomach



Muscle weakness, spasms or cramps



Dizziness, lightheadedness, fainting



Numbness in the hands and lips



Irregular pulse rate



Confusion

Safety visits will be performed during the study to identify and treat any change in blood potassium, in renal function or in blood pressure.

Please reference the Information Sheet for Parents/Guardians of Participants for the full list of side effects

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★ Explain that all drugs have side effects. One of the effects of the study drug can be the increase of blood potassium. This has been observed in the adult phase 3 studies about twice as often under the study drug treatment compared to placebo treatment (18.3% vs. 9% [FIDELIO DKD] and 10.8% vs. 5.3% [FIGARO DKD]). Hyperkalemia led to permanent discontinuation of treatment in 2.3% and 1.2% in the adult phase 3 studies, respectively, of patients receiving the study drug versus 0.9% and 0.4% of patients receiving placebo (see Protocol - Risk assessment 2.3.1). Hospitalization due to hyperkalemia for the study drug group was 1.4% and 0.6% in the adult phase 3 studies, respectively, versus 0.3% and 0.1% in the placebo group.

★ Let parents know that you will closely monitor any change in blood potassium with regular blood exams and that the dosage of the study drug will be slowly increased to lower the risk of hyperkalemia.

★ Remind parents that you will look out for any side effects. Let them know that you will provide them a telephone number to encourage parents and children to inform your team as soon as a side effect should occur.

★ Let parents know that the study will be monitored by a committee of independent experts that will review safety data and stop the study if they have any concern.

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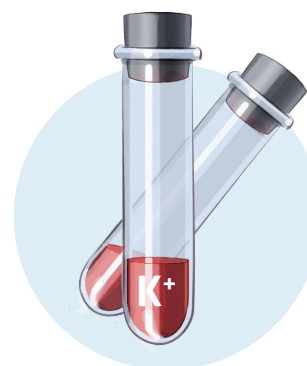
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- ☆ Help parents understand the meaning of multicenter, placebo-controlled, randomized and double-blind.
- ☆ Point out that other children will be involved in around 25 different countries.
- ☆ Let parents know that their child will have a 2 in 3 chance of getting the study drug and 1 in 3 chance of getting placebo.
- ☆ While discussing what double blind means, reiterate that, in case of an emergency, you can find out if the child is taking the study drug or placebo.


FIONA


What is the FIONA Study?

FIONA is a randomized, double-blind, placebo-controlled, multicenter study. It is sponsored by Bayer.




Multicenter

Multicenter means that the study will be conducted in many different hospitals. About 200 children will be involved in about 25 countries.



Placebo-controlled


To evaluate if the study drug works, it will be compared to a placebo treatment, a tablet or suspension (liquid) that will look like the drug but has no active medicine in it.



Randomized

To ensure fairness and accurate results, a computer will randomly choose (randomization) who takes the study drug and who takes placebo.

Your child will have a 2 in 3 chance (66%) of getting the study drug and a 1 in 3 (33%) chance of getting placebo.



Double-blind

No one (not you, the study doctor, nor the study sponsor) will know which treatment (study drug or placebo) your child will be taking until the study is over.

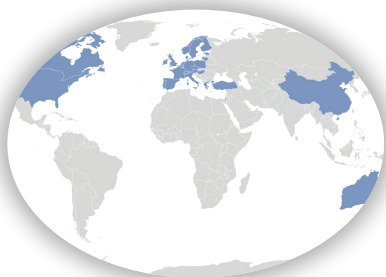
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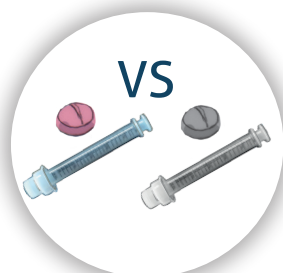
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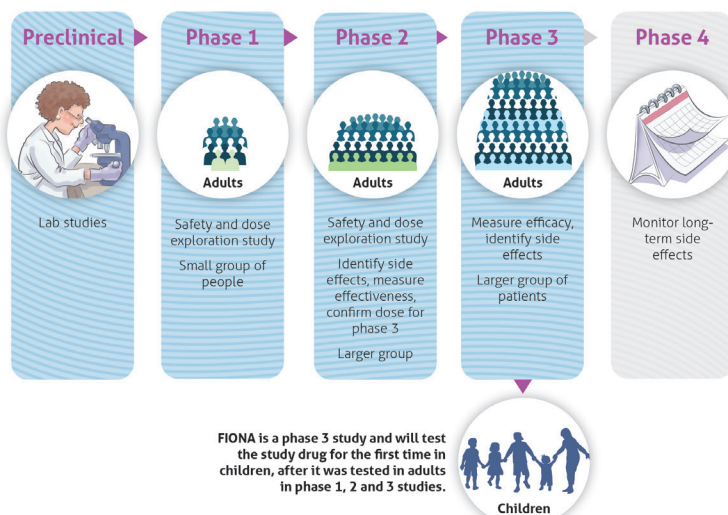
A phase 3 clinical study

FIONA is a phase 3 clinical study that aims to test if the study drug is effective and safe in children with CKD.

In phase 3 studies the treatment is given to a sufficiently large population of patients suffering from the disease for a detailed evaluation of the side effects and the efficacy. If the study drug successfully passes phase 3, it is ready to obtain approval by respective health authorities in each country.

The FIONA study will be evaluating 4 different age groups and will begin with the oldest age range and will be stepping down to the youngest age range.

Clinical studies progress through a series of steps (called phases) to test how well a drug or treatment works and how safe it is.



- ★ Explain that the study drug was tested in phase 1, 2 and 3 studies in adults.
- ★ Let parents know that the study will be evaluating 4 different age groups in children and will begin with the oldest age range and will be stepping down to the youngest age range. Age groups will be opened to participation as information is collected and evaluated by medical committees throughout the study.



What is the FIONA Study?

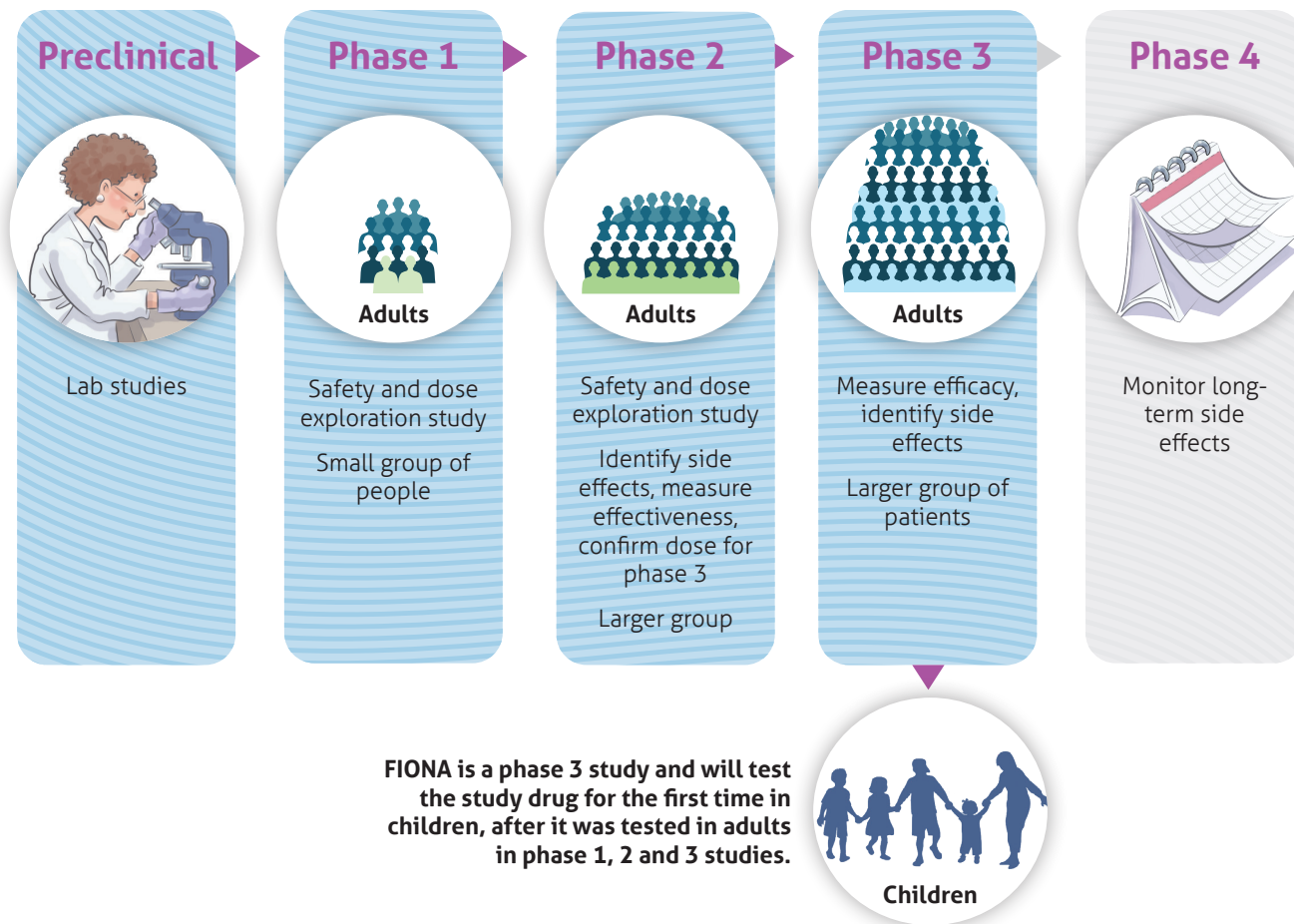
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What happens during the study?

Voluntary Participation

Participation in the FIONA study is voluntary.

If at any time and for any reason you want your child to leave the study, you are allowed to do so. Your child will continue to receive the standard of care treatment by his/her doctors even if he/she withdraws from the study.

Run-in visit

The study doctor will:

- ✧ Ask you if you agree to have your child participate in the study.
- ✧ If you agree, the study doctor will evaluate in detail whether your child is a candidate for the study. The doctor will check your child's medical history, weight and height, heart rate and blood pressure and perform blood and urine tests.
- ✧ The doctors will also check if your child is taking the optimal dose of blood pressure lowering drugs. If this is not the case, the doctor will adjust the drugs accordingly and check the dosage so that it remains stable for at least 30 days before starting the screening.



Screening visit

This visit may occur up to 3 months after the run-in visit (if there was a blood pressure lowering drug dose adjustment during the run-in visit). At this visit, the study doctor will check your child again, perform blood and urine tests and decide if he/she can participate in the study.

- ✧ Explain that taking part in the study is voluntary and that they can decide at any time to leave the study for any reason. Both the parents and the child (if age is applicable) must agree to participate.
- ✧ Let parents and children know that if they have doubts or questions it is totally normal, and that you and the other study staff are available to discuss these doubts now or at any time during the study.
- ✧ Discuss what will happen during the run-in and screening visits.
- ✧ Explain why you will perform these tests and that the results will be useful to decide whether their child can take part in the study.



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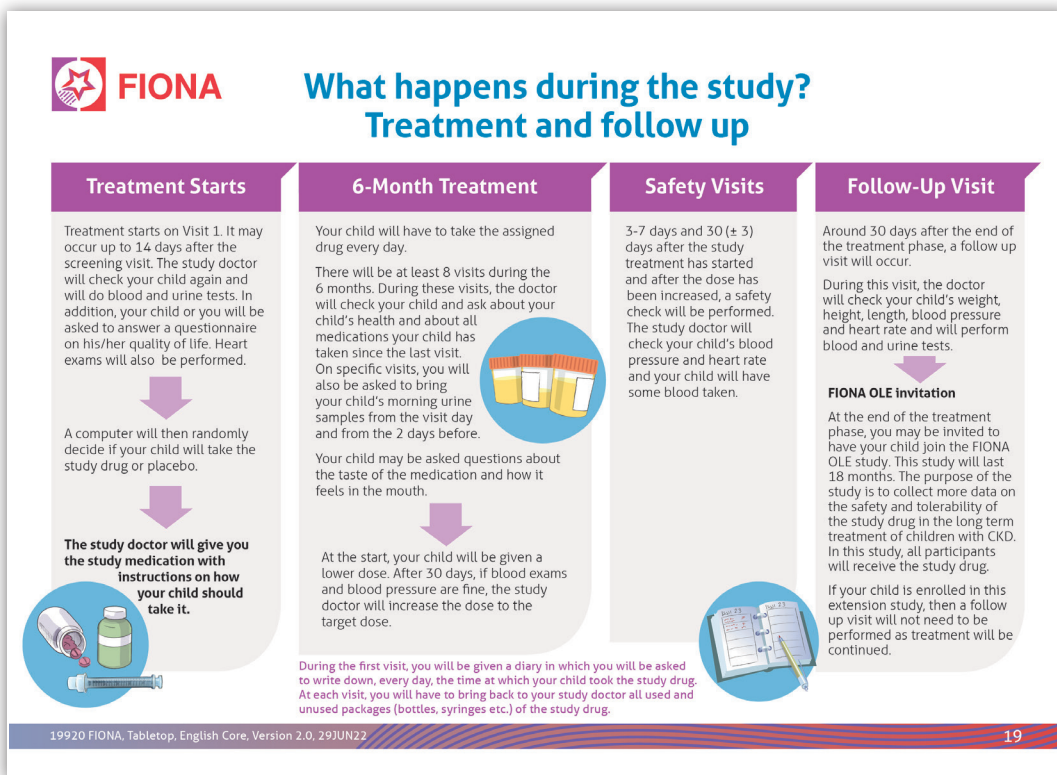
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- ★ Use this page to explain what will happen overall in the treatment and follow-up phase.
- ★ Let parents know that before treatment starts, a computer will randomly decide if their child will receive placebo or the study drug.
- ★ Explain when safety visits will be performed (after treatment initiation, up-titration or after restart of study treatment, in case of interruption).
- ★ Inform parents that after the treatment phase ends, they will be offered the possibility to let their child participate in the extension study called FIONA OLE.



What happens during the study?

Treatment and follow up

Treatment Starts

Treatment starts on Visit 1. It may occur up to 14 days after the screening visit. The study doctor will check your child again and will do blood and urine tests. In addition, your child or you will be asked to answer a questionnaire on his/her quality of life. Heart exams will also be performed.



A computer will then randomly decide if your child will take the study drug or placebo.



The study doctor will give you the study medication with instructions on how your child should take it.



6-Month Treatment

Your child will have to take the assigned drug every day.

There will be at least 8 visits during the 6 months. During these visits, the doctor will check your child and ask about your child's health and about all medications your child has taken since the last visit. On specific visits, you will also be asked to bring your child's morning urine samples from the visit day and from the 2 days before.



Your child may be asked questions about the taste of the medication and how it feels in the mouth.

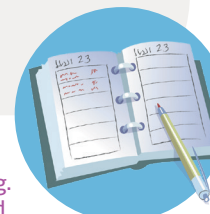


At the start, your child will be given a lower dose. After 30 days, if blood exams and blood pressure are fine, the study doctor will increase the dose to the target dose.

During the first visit, you will be given a diary in which you will be asked to write down, every day, the time at which your child took the study drug. At each visit, you will have to bring back to your study doctor all used and unused packages (bottles, syringes etc.) of the study drug.

Safety Visits

3-7 days and 30 (\pm 3) days after the study treatment has started and after the dose has been increased, a safety check will be performed. The study doctor will check your child's blood pressure and heart rate and your child will have some blood taken.



Follow-Up Visit

Around 30 days after the end of the treatment phase, a follow up visit will occur.

During this visit, the doctor will check your child's weight, height, length, blood pressure and heart rate and will perform blood and urine tests.



FIONA OLE invitation

At the end of the treatment phase, you may be invited to have your child join the FIONA OLE study. This study will last 18 months. The purpose of the study is to collect more data on the safety and tolerability of the study drug in the long term treatment of children with CKD. In this study, all participants will receive the study drug.

If your child is enrolled in this extension study, then a follow up visit will not need to be performed as treatment will be continued.



What happens during the study? Treatment phase - at home

During the treatment period, while at home, you will have the responsibility to ensure that your child takes the tablets or oral suspension as prescribed by the study doctor and to follow some specific instructions.

Taking the tablet or oral suspension

- ★ The prescribed tablets or oral suspension will have to be taken once, each day. On some visits, the drug will have to be taken during the study visit and not at home.
- ★ The tablets should be taken with a glass of water, with or without food (i.e. in the fed or fasted state). If your child is taking suspension, this should not be mixed into food before administration.
- ★ You will be given a diary on which to note, every day, at what time your child took the study drug.
- ★ You will also have to take note, in the diary, of any time your child spits out or vomits after taking the drug.



If your child will take oral suspension, after 30 days of taking the study drug and at the end of treatment phase, your child will be asked to answer questions on its taste. If your child is too young to answer these questions, you will be asked to reflect upon their facial expressions while taking the medication.

Your child must not eat any grapefruit nor drink any grapefruit juice during the treatment period.

Urine samples

Before most of the study visits, your child will have to collect morning urine samples for 3 days, one on the morning of the study visit day and the other 2 on the mornings of the previous 2 days. This will not be required before safety visits.



Contraception

If your daughter could become pregnant and/or is sexually active, she will have to adopt adequate contraception. The study doctor will provide more information on the required measures according to local laws and regulations.

If your daughter is of childbearing age, she will need to have a pregnancy test at the screening visit, after 90 days of treatment, at the end of study treatment and at the follow-up visit. In some cases, additional pregnancy tests may be required.



If your daughter is of childbearing age and misses a menstrual period/shows signs of pregnancy, you will have to let the study doctor know.

- ★ Discuss with parents and children what their child will have to do at home: coming to the scheduled visits, taking the study drug each day, collecting urine samples on some days and, if appropriate, ensuring female participants use contraception.
- ★ Check if parents or children expect to have any problem in the next 7-10 months that may interfere with participating in the study visits and following the study requirements.
- ★ Discuss the importance of contraception for adolescent females with childbearing potential.
- ★ Ask the female participant and/or her parents to inform you if she/their daughter has her first period while in the study and/or intends to become sexually active, and to let you know if she misses a menstrual period or shows signs of pregnancy.
- ★ Inform parents and children that during the treatment period the participant must not eat any grapefruit nor drink any grapefruit juice because these foods have an impact on the levels of study drug in the body.

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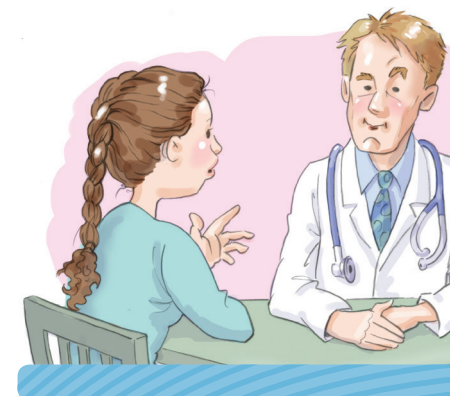
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FIONA

What happens during the study? Assessing safety and efficacy

During the study your child will undergo several medical assessments. These assessments will help doctors evaluate if the study drug is safe, if it is working in your child's body and how the body responds to the treatment.




ALL VISITS

Blood tests

Blood samples will be taken from a vein, usually in the arm.

Blood tests will mainly check:

- the kidneys' ability to filter waste by measuring the amount of a waste, called creatinine, in the blood. The study doctor will assess your child's creatinine levels to calculate the glomerular filtration rate (eGFR). Serum creatinine and eGFR indicate how much waste the kidneys can filter.
- the levels of potassium.
- how the study drug acts on the body and how the body affects the study drug.




MOST VISITS

Urine tests

Urine tests help doctors assess:

- the kidneys' ability to keep proteins in the blood by measuring how much protein is lost in the urine. The amount of proteins is then compared to the amount of creatinine in the urine (**urine protein to creatinine ratio or UPCR**).



ALL VISITS

Vital signs

The study doctor will check your child's heart rate, temperature and blood pressure.

Blood pressure will be measured 3 times. Your child will rest for 5 minutes before the first measurement and for at least 3 minutes in between measurements. Blood pressure is checked to help ensure it is not too high or too low and to evaluate if the study drug has an effect on it.

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- Use this page to help parents understand why blood and urine tests are performed and why vital signs are checked. You can go back to the pages on CKD and on CKD stages to better explain why creatinine and urine protein are assessed.
- Let parents know that we will compare the creatinine/eGFR and urine protein values of the children taking the study drug to that of the children taking placebo.
- Explain that blood tests will be done also to check blood potassium and to assess how the study drug acts on the body and how the body affects the study drug.

What happens during the study?

Assessing safety and efficacy

During the study your child will undergo several medical assessments. These assessments will help doctors evaluate if the study drug is safe, if it is working in your child's body and how the body responds to the treatment.

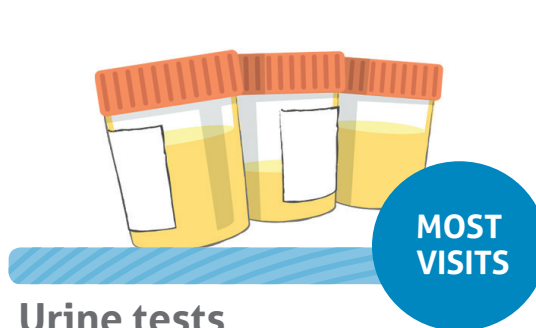


Blood tests

Blood samples will be taken from a vein, usually in the arm.

Blood tests will mainly check:

- ✧ the kidneys' ability to filter waste by measuring the amount of a waste, called creatinine, in the blood. The study doctor will assess your child's creatinine levels to calculate the glomerular filtration rate (eGFR). Serum creatinine and eGFR indicate how much waste the kidneys can filter.
- ✧ the levels of potassium.
- ✧ how the study drug acts on the body and how the body affects the study drug.



Urine tests

Urine tests help doctors assess:


- ✧ the kidneys' ability to keep proteins in the blood by measuring how much protein is lost in the urine. The amount of proteins is then compared to the amount of creatinine in the urine (**urine protein to creatinine ratio or UPCR**).



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FIONA

What happens during the study? Assessing safety and efficacy

During the study your child will undergo several general and specific medical assessments. These assessments will help doctors evaluate if the study drug is safe, if it is working in your child's body and how the body responds to the treatment.

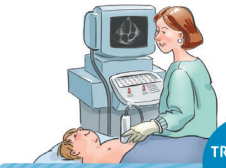


SOME VISITS

Electrocardiogram

An electrocardiogram (ECG) is an examination that helps doctors check the heart's rate and rhythm. Patches/ electrodes are applied to different parts of your body (usually chest, arms and legs) to record your heart's electrical activity.

This test is performed to identify any problem in the heart rhythm, and, if your child has very high blood potassium levels, to identify any effect of this on the heart activity.




AT TREATMENT START AND END

Heart ultrasound

Heart ultrasound (or echocardiography or echocardiogram) is an imaging test that uses ultrasound waves to make moving pictures of the heart. During this test, a gel and an ultrasound probe are put on your child's body.

This exam is performed because children with CKD are at risk of having heart problems.



AT TREATMENT START AND END

Quality of life questionnaire

You or your child will be asked to answer a questionnaire on your child's quality of life.

Answers to this questionnaire will help doctors check if the patients taking the study drug experience an influence in their quality of life, compared to patients taking placebo.

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- ★ Use this page to help parents understand why the heart exams are done.
- ★ Discuss with parents the fact that children with CKD are also at higher risk of having heart diseases and that the ECG and heart ultrasound may help identify heart problems before symptoms arise.
- ★ Inform parents that they or their child will have to answer questionnaires on the study drug's taste and texture and on their child's quality of life. This will help check if the study drug's taste is acceptable and if taking the study drug has an influence on the quality of life.

What happens during the study?

Assessing safety and efficacy

During the study your child will undergo several general and specific medical assessments. These assessments will help doctors evaluate if the study drug is safe, if it is working in your child's body and how the body responds to the treatment.

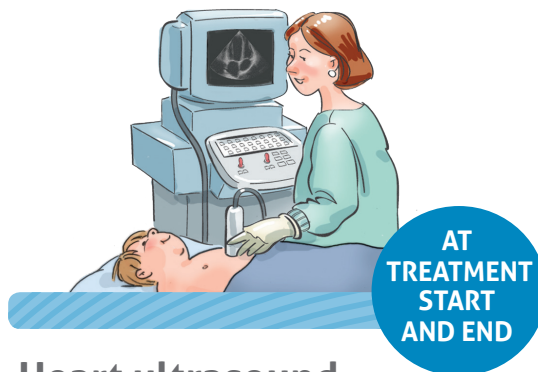


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What happens during the study? The study visits schedule

AT EVERY STUDY VISIT: the doctor will check which drugs your child is taking or took in the past. **During treatment**, the doctor will also check at each study visit if your child had any side effects and will review the patient diary with you. The study doctor or nurse will collect all unused study medication, bottles, etc. and

dispense new ones if required.

AT SOME STUDY VISITS: doctors will also perform additional assessments or procedures (indicated with a star in the table below).

Study visit	Run-in	Screening	1	2	3 (UT)	4 (SV)	5 (UT)	6 (SV)	7 (UT)	8 (SV)	9 (SV)	10	Follow up
When	Up to 3 months before screening	Up to 14 days before visit 1	Day 0	Day 3-7	Month 1		Month 2		Month 3			Month 6	Month 7
Informed Consent	*												
In/Exclusion	*	*	*										
Physical examination		*	*									*	
Vital signs*	*	*	*	*	*	*	*	*	*	*	*	*	*
Blood test	*	*	*	*	*	*	*	*	*	*	*	*	*
Randomization			*										
Demography	*												
Medical history	*	*											
Weight	*	*	*		*		*		*			*	*
Height/Length	*	*	*		*		*		*			*	*
Questionnaires (quality of life/drug taste)			*		*							*	
Urine test	*	*	*		(*)		(*)		*			*	*
ECG			*		*		*		*		*	*	
Heart ultrasound			*									*	

(*) : test may not apply because obtaining urine samples in incontinent children may not be possible so frequently.

*Vital signs: temperature, blood pressure and heart rate; UT: Up Titration visit; SV: Safety visits. These visits will occur after the start of the study drug and if the dose is increased at the previous Up Titration visits (3, 5, or 7). Safety visits can also occur any time after restarting the treatment after a suspension period.

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✧ This page depicts a simplified version of the study schedule of activities. You can use it to help parents and children understand how many visits will occur, how much time the study will last and what will happen at each visit.

✧ Let them know that safety visits will occur only after the start of the study treatment, if in the previous visit the study drug dose was increased or if it was restarted after an interruption.



What happens during the study? The study visits schedule

AT EVERY STUDY VISIT: the doctor will check which drugs your child is taking or took in the past. **During treatment,** the doctor will also check at each study visit if your child had any side effects and will review the patient diary with you. The study doctor or nurse will collect all unused study medication, bottles, etc. and

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Informed Consent	☆												
In/Exclusion	☆	☆	☆										
Physical examination		☆	☆									☆	
Vital signs*	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆
Blood test	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆	☆
Randomization			☆										
Demography	☆												
Medical history	☆	☆											
Weight	☆	☆	☆		☆		☆		☆			☆	☆
Height/Length	☆	☆	☆		☆		☆		☆			☆	☆
Questionnaires (quality of life/drug taste)			☆		☆							☆	
Urine test	☆	☆	☆		(☆)		(☆)		☆			☆	☆
ECG			☆		☆		☆		☆		☆	☆	
Heart ultrasound			☆									☆	

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Take time to make your decision.

You can read through all the material that the study staff has provided and ask your study doctor questions if you have any. Encourage your child, if old enough, to discuss his/her doubts and talk with the study doctors and nurses before making a decision.



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- ✧ Let parents and children know that they can take their time to make a decision.
- ✧ Reassure them that you are available to answer any questions they may have.
- ✧ Check if you have given them all the patient material for the age group (parent booklet and any preconsent children's booklet) and invite them to read the material and come back to you if they have additional doubts or questions.
- ✧ Remind them that, once in the study, they can decline participation at any time without giving specific reasons, and that they will continue to receive standard of care.



Take time to make your decision.

You can read through all the material that the study staff has provided and ask your study doctor questions if you have any.

Encourage your child, if old enough, to discuss his/her doubts and talk with the study doctors and nurses before making a decision.

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ADDITIONAL SECTION for sites using the study app

At sites where local regulations permit remote visit activities, you will have the possibility to use a study app and to perform some study visits from home (Visit 2, 7 and the follow up).

A nurse will come to your home to take the necessary blood and urine samples. You will then connect with the study doctor through a remote telehealth call to discuss the results of the exams.

The study app will support your study journey with:

- ✧ reminders/notifications of each study activity
- ✧ online surveys and questionnaires
- ✧ scheduling and telehealth video calls with the study doctors.



- ✧ Use this page only if the study app and decentralized clinical trial is approved in your country and site.
- ✧ Let parents know of the possibility of conducting some visits at home and of having a study app with reminders and scheduling functionalities.

**PLEASE DO NOT USE THIS PAGE AND REMOVE THE FOLLOWING SHEET FROM THE TABLETOP FLIPCHART
IF NOT APPLICABLE AT YOUR SITE**



ADDITIONAL SECTION for sites using the study app

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