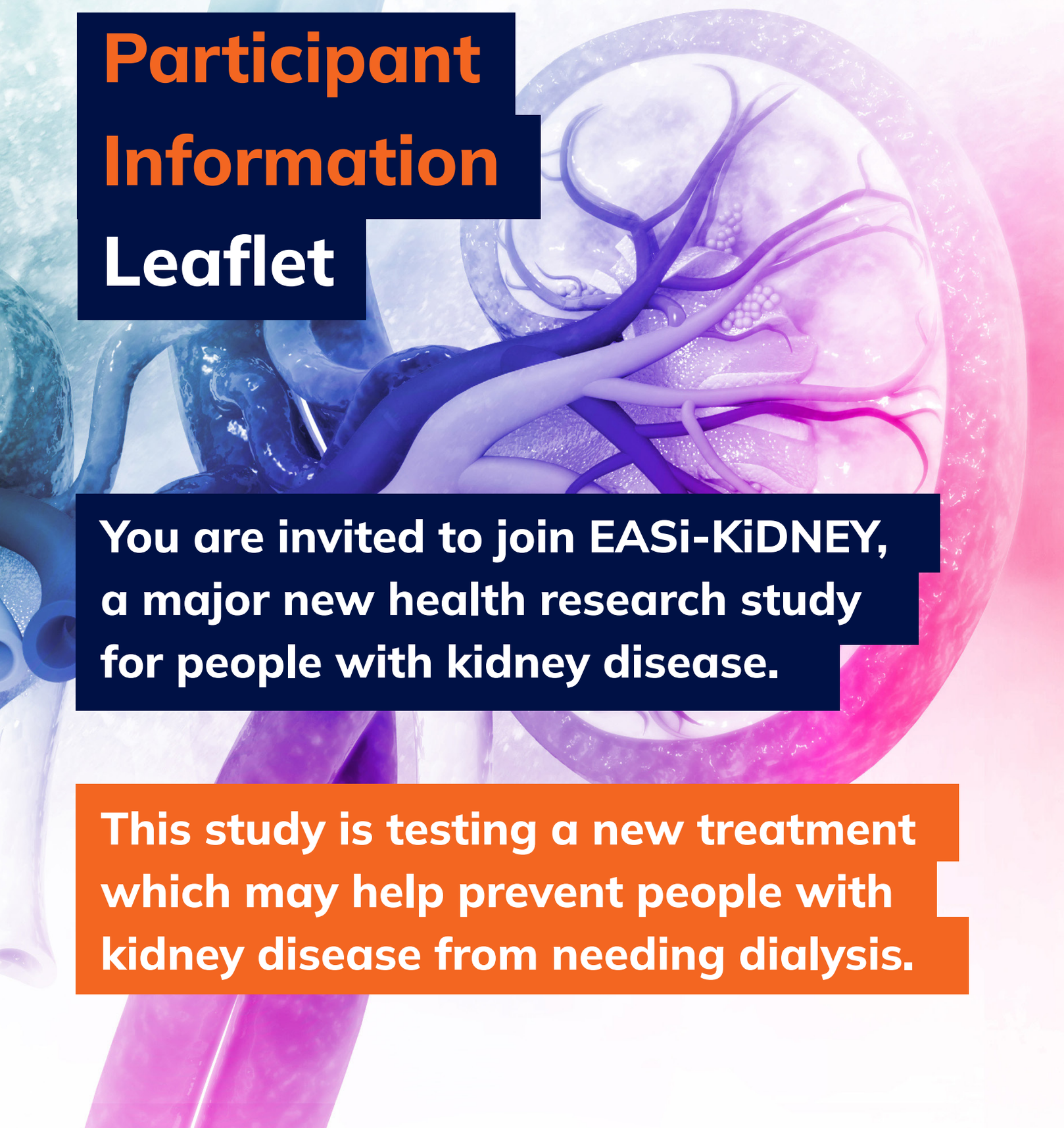
EASi-KIDNEY

Aldosterone Synthase inhibition & Empagliflozin in CKD

Participant Information Leaflet



You are invited to join EASi-KiDNEY, a major new health research study for people with kidney disease.

This study is testing a new treatment which may help prevent people with kidney disease from needing dialysis.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Contents

EASi-KIDNEY: Summary

- You are invited to join an important new health research study called EASi-KIDNEY, led by scientists at **Oxford Population Health**, part of the University of Oxford. It is entirely up to you if you take part or not;

- EASi-KIDNEY is testing whether taking a new medication currently called BI 690517, taken in combination with a well-tested medication called empagliflozin, lowers the risk of worsening kidney disease or heart disease in patients with kidney disease;

- In a previous large clinical trial conducted by Oxford Population Health, empagliflozin was shown to reduce the risk of needing dialysis or a kidney transplant or death from cardiovascular disease in people who had kidney disease and is now recommended for most adults with chronic kidney disease worldwide;

- Empagliflozin (and other similar drugs ending in **–flozin**) reduce the need for dialysis but are not a cure and the risk of this remains higher for many people with kidney disease. Therefore, we need to test additional treatments;

- BI 690517 is a newly-developed drug which may counter the harmful effects of a chemical called aldosterone which is known to accelerate worsening of kidney and heart disease and cause high blood pressure;

  If you agree to take part, you will be joining about 11,500 other volunteers;

- Every participant will get empagliflozin and in addition, half will get BI 690517 and the other half will get an inactive dummy pill (known as placebo), all to be taken once a day. Which treatment you receive is decided by chance and neither you nor the study team will know which treatment you are given;

- Joining the study involves attending five clinic appointments in about the first six months and then an appointment once every six months. At each appointment a trained researcher (usually a research nurse) will ask you some questions about your health and give you a supply of study pills;

- Because kidney disease is identified and tracked by blood and urine tests, at each appointment you will be asked to provide a blood and occasionally a urine sample (even if you stop taking your study pills);

- You are asked to stay in the study for about three to four years. It needs to be this long to make sure this study is a definitive test of BI 690517 on kidney disease which often takes several years to progress;

- We would like to also use medical and civil registration records (eg those maintained by NHS England, the NHS Diabetic Eye Screening Programme [if you have diabetes], and the UK Renal Registry) to follow your progress;

- If you join the study, your GP will be informed and your usual medical care will not be affected by taking part;

- The University of Oxford is running the study. Study pills and a grant to run the study have been provided by Boehringer Ingelheim International GmbH (the drug company who make empagliflozin and BI 690517, and who are known as the sponsor).

If you would like to find out more, please read the rest of this leaflet carefully.

Kidney disease is common and linked with heart disease

Chronic kidney disease (CKD) is a common condition, affecting about one in ten people worldwide. It is diagnosed and monitored by means of blood and urine tests.

CKD is caused by many different things, including increasing age. Diabetes, high blood pressure, inflammation in the kidney, and inherited diseases are the most common causes.

It is known that people with kidney disease are both at risk of their kidney problem worsening and developing heart problems.

New treatments for kidney disease and heart disease are needed

20 years ago, a group of medications which block a biological system, called the renin-angiotensin system (RAS), were shown to protect the kidney and the heart. Because of these clinical trials, these medications are now used widely. (You may be taking one: their names end in **-pril** or **-sartan**.) These simple treatments have meant some people have not needed to start dialysis and they have saved lives.

In recent years, drugs ending in **-flozin**, such as empagliflozin (known as sodium-glucose cotransporter-2 [SGLT2] inhibitors) have been found to further slow the worsening of kidney disease in addition to RAS inhibitors.

However, despite taking RAS inhibitors and SGLT2 inhibitors, many people with kidney problems continue to develop worsening of their kidney disease and/or heart problems. Scientists are searching for new treatments to reduce the remaining risk of kidney and heart problems in people with kidney disease.

There is now a new medication called BI 690517 which may have further benefits for people with kidney disease, in addition to RAS inhibitors and SGLT2 inhibitors. Evidence has recently emerged from early trials that BI 690517 reduces the amount of protein in the urine (a marker of kidney damage) in people with kidney disease - a sign that it might also reduce the need for dialysis longer-term, though this needs to be tested in a large trial.

What is the treatment being tested?

BI 690517 is a recently-developed drug which acts to block an enzyme (a hormone-making protein) in your body called aldosterone synthase. Aldosterone synthase produces aldosterone, a hormone that is elevated in people with CKD, increases blood pressure and we believe may also increase the risk of worsening kidney disease. It can also damage the heart. By reducing the body's aldosterone levels, there may be a benefit to both your heart and kidneys over the long term.

BI 690517 has not yet been approved as a treatment for any disease and therefore its use in this clinical trial is considered experimental. It has previously been tested in clinical trials with healthy volunteers and in a small number of patients with kidney disease to determine the most appropriate dose to use in large trials like EASi-KIDNEY.

In EASi-KIDNEY, BI 690517 will be tested in combination with empagliflozin, an SGLT2 inhibitor which has already been proven effective and safe in patients with CKD in the EMPA-KIDNEY trial, a previous trial conducted by Oxford Population Health and a committee of international experts (www.empakidney.org). Empagliflozin causes blood sugar (equivalent to 10 teaspoons a day) and salt to pass into the urine. This slows the worsening of kidney disease and also results in a modest fall in body weight and blood pressure.

What is the key question the study will answer?

EASi-KIDNEY is a clinical trial which follows the success of EMPA-KIDNEY. EASi-KIDNEY is also being led by Oxford Population Health. The scientists in Oxford want to find out whether taking BI 690517 in combination with empagliflozin every day prevents worsening of kidney disease or deaths from heart disease in people who have kidney disease.

The reason for testing the combination of these two drugs is to be able to test whether the addition of the new treatment BI 690517 is more effective than empagliflozin alone. Because empagliflozin has been shown to safely slow the progression of kidney disease in EMPA-KIDNEY, all trial participants will be provided and treated with empagliflozin throughout the EASi-KIDNEY trial.

Why me?

Your doctor has reviewed existing blood and urine test results which show some evidence that you have had protein in your urine or reduced kidney function in the past. You are probably already aware of this, but you may not be, and it is also possible that the protein in your urine or reduced kidney function is no longer present.

You have been invited to a study appointment to test your blood and urine again, and to discuss taking part in the study. The scientists need a range of people to join the study, including those with only early signs of kidney disease risk as well as people who have already seen a kidney doctor.

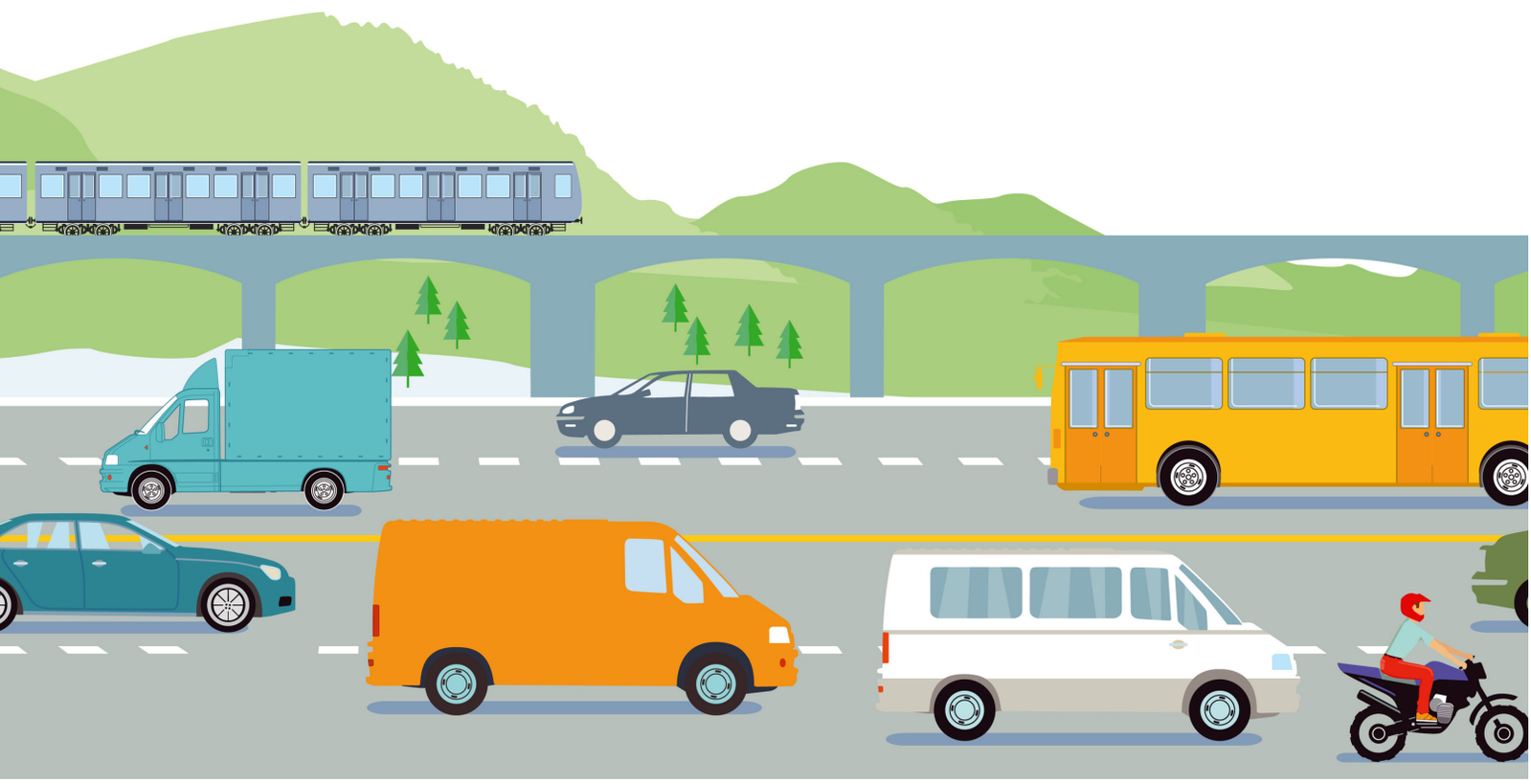
Do I need to take part?

No, you do not have to take part in this trial. It is entirely your decision. It is important to be aware that if you join this study, it will not affect any decisions about other medical treatment you might need or be receiving from your own doctors.

If you do decide to come to the first study appointment, you will be given an opportunity to ask questions about the study. Once we have checked your blood and urine tests, we will also check with the hospital doctor leading the trial in your hospital or GP practice that they think you are appropriate to join the study. We will also tell your hospital or GP practice that you wish to take part.

By joining this study, you will become part of our efforts to save the lives of people with kidney problems and hopefully reduce the need for kidney dialysis in years to come.

Travel expenses



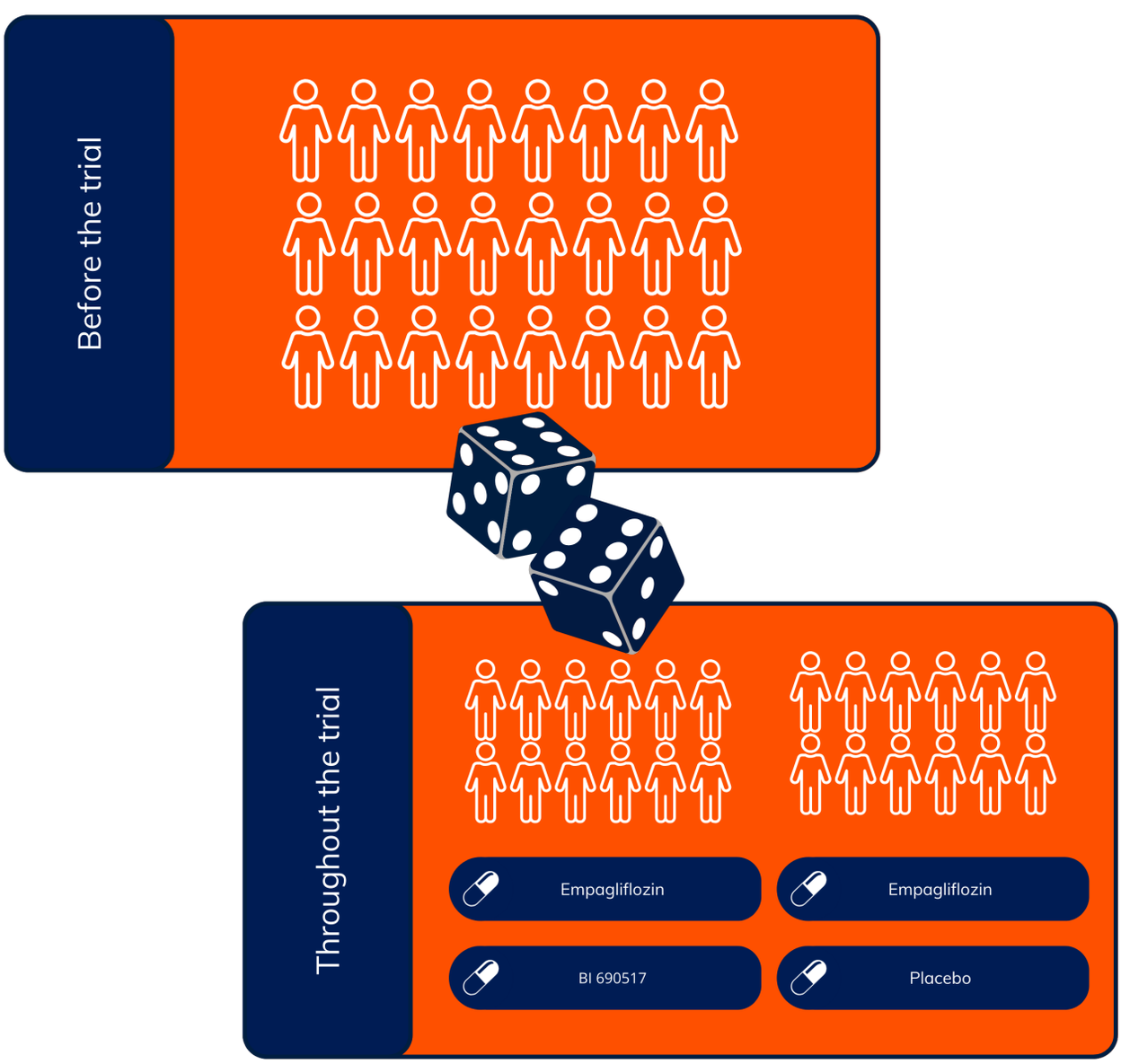
The study can pay you back for all reasonable costs for travelling to your study appointments (eg car parking and petrol or other transport costs). Please make sure you ask at the clinic.

Otherwise taking part in the study is voluntary and you will not receive payment for your participation (ie you are donating your time, information about your health, and samples of your blood and urine).

Who decides what treatment I get?

Everyone taking part will receive empagliflozin. In addition, half the people taking part in this study will get the active BI 690517 pill and half will get the dummy inactive pill (known as placebo). Which treatment you get will be decided by the computer by chance (like tossing a coin). This is called randomisation.

Neither you nor your doctors will know which treatment you are given and the study staff will not know either. This ensures the study gives results that are reliable and trustworthy.



Are there any alternative treatments?

During the study you should continue to take any other treatments you may have been given to treat your kidneys. Your local doctors will be asked to ensure they continue to treat your other medical problems according to guidance produced by experts at a local, national or international level.

If you are already taking any medication with the name ending in -flozin [such as dapagliflozin or canagliflozin), you will have to stop this and switch to empagliflozin to be able to join this study.

Your local study doctors will be asked to review the information collected at your first study visit (the screening visit) and approve your entry into the trial.

They will consider whether you may need to start a treatment called finerenone, which is similar to BI 690517, and can be used in certain patients with diabetes and chronic kidney disease.

If you are taking or are recommended to start finerenone (or any similar type of drug such as eplerenone or spironolactone), you will not be able to take part in EASi-KIDNEY.

What will I have to do?

For EASi-KIDNEY to be able to give reliable results, it is important that people stay in the study and take their study pills (both types) every day for about three to four years, wherever possible.

The study needs to be this long so it is a definitive test of the effects of the pills on kidney disease, which can take years to progress. The results of the study could have a major impact on how kidney patients around the world are treated.

By joining the study, we are asking you to attend the local study clinic five times in about the first six months, and then attend every six months after that for a total of three to four years.

At each study appointment, a trained researcher (usually a nurse) will ask you about your health and give you a new supply of study pills. You will then have a blood sample taken to monitor your kidneys and other effects of the study pills.

At a small number of visits, we will also ask you to provide a urine sample. In addition, we may send you a questionnaire about 'how you feel and your quality of life' by post or email.

With your permission, we would also like to store left over blood and urine for future scientific research, including tests on your genes. This part of the study is optional, so you can still participate in the study even if you do not want your left over blood and urine stored long-term.

What happens at the first appointment?

At your first study appointment (called your screening visit), with your agreement, a trained study nurse (or research coordinator) will check your previous blood and urine test results and then explain the study to you. You will have plenty of time to ask questions.

You will then be asked to sign a consent form if you agree to take part. The study nurse will then ask some more details about your medical history and current medication. They will also take a fresh blood sample (about one teaspoonful) and collect a urine sample to be sent to the local laboratory for testing.

The study nurse will ask for a list of medications you are currently taking. If you are not currently taking empagliflozin, you will also be prescribed this and required to take empagliflozin for the duration of the study. If you are already taking a similar drug (another type of SGLT2 inhibitor which ends in -flozin), you will be required to stop taking this and switch to empagliflozin instead. Empagliflozin will be supplied as part of the trial for the full duration of the trial.

This first appointment is one of the longest appointments and could take up to an hour to complete. If you are willing and able to take part in EASi-KIDNEY, the study research nurse will give you a supply of pills to take for two to three months to see if taking these extra pills every day is acceptable to you.

After this appointment you are then in what is called the run-in phase. During this time, you will be advised to start taking the second study medication called empagliflozin alongside the other treatment BI 690517 or placebo. If you are already prescribed an alternative SGLT2 inhibitor (-flozin) medication, you will be instructed to stop taking this and switch to empagliflozin after discussion with your doctor. The study nurse and doctor will give you clear instructions. The research team will also write to and inform your GP to let them know that you are planning to join the EASi-KIDNEY trial.

You will be given a participant card with the contact details of the study team so that your clinical team can promptly report all hospitalisations and emergencies.

What happens at the second appointment?

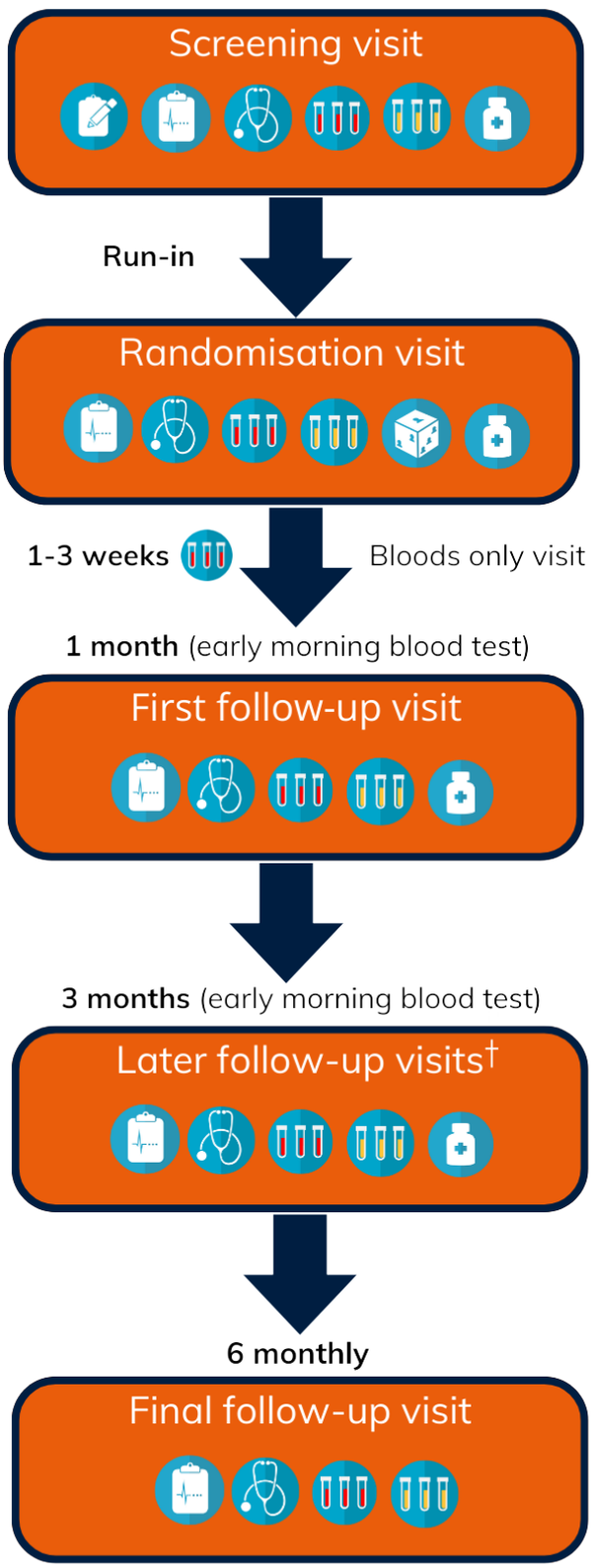
Two to three months later, you will have your second appointment (called your randomisation visit). At this appointment we will check how you got on taking the study pills. You will also be asked if you remain willing to commit to the study for around three-four years.

If you are happy to join, the study team will perform a short interview, collect another blood sample (about six teaspoons this time), ask you to provide a urine sample, and give you your next set of study pills. This should only take 30-45 minutes.

What happens next?

You will have another appointment 1-3 weeks later (**bloods only** visit) at which you will have a blood sample taken (between 3-6 teaspoons) to check the levels of components in your blood (including potassium), which can be affected by the study treatment. This is to test for any early potentially harmful effects of the study treatment. Your local doctor will be informed if these results are abnormal and require action, otherwise you will not be told the results of these tests. This visit will be shorter than other study visits as it is not necessary to complete health questions or undergo physical measurements like at other visits.

EASi-KIDNEY visit schedule



Key	
	Consent form
	Questions about the pills and your health
	Physical measurements (eg blood pressure)
	Bloods sample
	Urine sample
	Randomisation to BI 690517 or placebo
	New supply of study pills provided

† Urine test and provision of saliva pots at 18-month visit only

What happens at the other appointments?

Your next two appointments (called **follow-up** visits) will be about one month and three months after your second study visit (your **randomisation** visit).

The blood tests taken for these first two follow-up visits will include a check of the levels of stress hormone cortisol in your blood. It is important, wherever possible, that the blood test for these two visits are taken **early in the morning** (ideally before 09:00) to ensure the results of a cortisol test can be reliably interpreted. Taking samples after 09:00 might mean they need to be repeated and we want to avoid this inconvenience for you wherever possible. We appreciate your co-operation with timing of appointments.

You will not be given any study pills at the one month **follow-up** visit. At the three month **follow-up** visit you will be given another supply of study pills and the study research team will see you three months later and then every six months. Blood sampling will usually not be required to be before 09:00 at subsequent visits.

Note that only at the one month and three month visits will you need to have early morning (ideally before 09:00) blood tests. However, your contribution to the study could be even more valuable if you would be willing to have early morning blood tests at every study visit. This would allow us to learn about any changes in hormone levels caused by study pills but is an **optional** part of the study.

At each six-monthly **follow-up** visit, the study team will ask you about any new medical problems since your last appointment, give you the next supply of study pills, and take a blood sample (between three to six teaspoons each time), and possibly a urine sample. Each follow-up visit is designed to ideally take less than 30 minutes (although the time needed to collect blood samples and dispense study pills can vary from hospital to hospital).

Following your last trial Follow-up visit, you will stop the study pills.

What if I don't want to carry on with the study?

We hope you will be able to continue to take the study pills for the full course of the study.

For the study to produce reliable results, it is necessary for participants to remember to take their study pills as best they can, and for the study team to collect complete information about the health of as many participants as possible.

Your participation is voluntary. It remains your right to decide you no longer wish to, or are no longer able to, participate in any aspect of the study at any time. All data as well as blood and urine samples already collected from you until the time you stop participating in the study will be kept and used as described below.

If you withdraw, your usual rights as an NHS patient will not be affected in any way.

If you are asked to stop your study pills by a doctor, or you choose to stop them yourself, it is important that the study team can stay in touch with you and you continue to attend study visits. To make sure the study produces reliable results we would also need, wherever possible, to continue to collect blood samples at the study clinics for the full trial duration (three to four years).

You may decide that you really do no longer wish to come to the study clinic. We would want to keep in touch by other methods. There is more detail in the accompanying **Data Protection Information Leaflet**.

Blood and urine samples

The blood samples you provide will be used to measure things such as kidney, liver, heart function, steroid hormones, and levels of blood sugar and salts in your body. We will also measure levels of BI 690517 in your blood. The study team want to measure these things to assess the effects of the study pills.

The urine samples will be measured for protein markers of kidney disease and damage.

Some of these tests are not routinely performed by all hospitals and ideally all samples need to be measured in a single laboratory, so some of your blood and urine will be transported to Oxford. This is why study blood and urine samples will need to be taken at the study appointments rather than at a different place (such as your GP practice).

The study research team will also ask you if you would allow leftover blood and urine samples, together with your health data collected in this study, to be stored long-term to help investigate other effects of the study medications and other future research (see below).

Leftover blood and urine samples are those which have already been collected for the purposes of the study, and would be discarded otherwise. There is no additional health risk to you. You can choose whether or not you would like to participate in this optional part of the study. If you decide that you do not want to give permission, you can still take part in the main part of the study.

How much blood will be taken?

The amount of blood will vary at different times during the study but will usually be between three and six teaspoons of blood each time.

Stored samples and future research

Doctors already know about some of the causes of kidney disease and heart disease. Scientists also think that other factors might play a part, but there is limited understanding of how they work.

In particular, we have limited knowledge about the effect of genes/DNA on the risks of kidney disease, heart disease, strokes, diabetes, and a range of other health problems that might be linked to these diseases. These include diseases that your doctor might refer to as metabolic, cardiovascular, infectious, or malignant diseases.

Please note that neither you nor your doctors will be given any information from the analysis of blood and urine samples, including any details of your genes/DNA. In particular, having these samples stored and tested will **not** affect your ability to get medical or life insurance at any time.

If we have your permission to keep your samples, then in the years to come we might be able to make new scientific discoveries using both the information collected in the study and by defrosting and analysing your samples (including testing some or all of your genes/DNA).

With your consent, the blood and/or urine samples will be stored in a freezer overseen by the University of Oxford for up to 30 years after the study is completed, and will then be destroyed. For details on how your blood and urine samples will be stored please see the accompanying **Data Protection Information Leaflet**.

What are the benefits of taking part in this study?

It is not yet known whether the trial drug will improve your kidney disease so you may not personally benefit from participating in this trial, but you will contribute new information that may benefit other patients and provide the medical and scientific community with information about treatments

for chronic kidney disease. In addition, your kidney disease will be more closely monitored during this trial which may be beneficial. If the medication combination is shown to have benefits, results from this study may help to prevent deaths from heart disease and the need for dialysis or transplantation around the world.

Please note that you are donating your time, information and blood/urine samples, for which we are grateful, but you or your relatives will not be able to receive any financial benefits from any discoveries or products developed using the results from this study or any future research using your health information and data.

Are there any risks?

Most treatments have side effects, which some people may experience, and others may not. EASi-KIDNEY is testing BI 690517 in combination with empagliflozin and both medications have different potential side effects. Importantly, we think the two tablets taken together may reduce the chances of raised potassium levels with BI 690517 (more details below).

Potential side effects of empagliflozin

Empagliflozin has already been tested in over many thousands of people with and without chronic kidney disease and is generally well-tolerated. It now has a licence from health regulators for use in certain types of people who have type 2 diabetes, and people with heart failure or chronic kidney disease (with or without diabetes). Nevertheless you may experience some symptoms when taking empagliflozin due to the way the drug works in the body.

For example, **empagliflozin causes increased salt and water loss into the urine** and some people report noticing a **need to pass urine more often initially**. Some have reported symptoms suggestive of **dehydration**, such as increased levels of **thirst** or **feeling faint**. **Constipation** can also happen as a result of dehydration. It may be necessary to change some of your other pills to compensate if these symptoms occur.

Empagliflozin also works by increasing sugar in the urine. This can occasionally cause pain on passing urine and/or increase the chance of **fungal genital tract infections, like thrush**. Such infections are usually easily treated with a cheap topical cream (occasionally it may require a course of antifungal pills). Urine infections have been reported and may require a course of antibiotics. If such treatment is ever needed, your GP or local research team will help diagnose and treat you. In uncommon circumstances, the urine infection may be severe and require treatment in hospital with antibiotics through a drip. In exceedingly very rare circumstances, such infections can become serious and spread to the area around the anus and genitals. **Please contact your doctor immediately if you develop any symptoms of pain, tenderness, redness or swelling of the genital area.**

Low blood sugar may also occur, almost exclusively in people with diabetes who are already taking insulin or certain diabetes pills (like gliclazide). Common low blood sugar symptoms include: **sweating, shakiness, hunger, restlessness, slurred speech,** and **confusion.** A sugary drink normally reverses the problem.

For people with diabetes, there is a risk of a condition called **ketoacidosis**. If you have had ketoacidosis in the last five years you cannot join the trial. Ketoacidosis is caused by a build up of ketones that occurs if there is too little insulin in the body. This can happen if the blood sugar is high but also even when your blood sugar is normal. The symptoms of ketoacidosis are non-specific, including **feeling or being sick, tummy ache,** and **shortness of breath**. Others may notice the **smell of pear drops or nail varnish remover on your breath**. Ketoacidosis is treated with insulin and fluid intake. Ketoacidosis can sometimes be life-threatening (if not appropriately treated) and may need hospital treatment with a drip and insulin. Ketoacidosis can rarely occur in people without diabetes, and is triggered by restricted food intake or severe dehydration. You are therefore instructed to stop your study pills if you are ever unable to eat (such as waiting for an operation in hospital) or generally unwell because of an acute illness. If you intermittently fast (such as for Ramadan) then please discuss this with your study team and follow local guidance.

If new information is learnt about empagliflozin during the trial, we will share it with you in a new leaflet.

Potential side effects of BI 690517

BI 690517 has been studied in an initial trial in about 700 patients with chronic kidney disease for about 14 weeks. That study provided important information on safety of BI 690517 in people with chronic kidney disease that informed the design of EASi-KIDNEY and the blood monitoring that is required.

BI 690517's main side effect is that it can cause an **elevation in the levels of potassium** (K+, a kind of salt) **in your blood**. Your potassium levels will be checked at every study appointment. High potassium usually does not result in any symptoms. Particularly high potassium can however cause temporary muscle weakness and heart palpitations. If you develop high potassium levels in the blood, the study team will discuss this with you and advise you to modify your diet according to the advice in the accompanying **Dietary Potassium Leaflet**. The study team may also adjust some of your existing tablets or start additional treatments to manage your potassium if required.

Dehydration can cause a temporary fall in kidney function (known as acute kidney injury). Because of this, it is important that you drink adequate water (especially in hot weather) and alert your doctor if you produce less urine than normal.

Your blood pressure will be monitored at each study visit as the treatment can **lower blood pressure**. If required, adjustments to other non-study blood pressure treatments might be made by your local study doctors.

We will be **monitoring your stress hormone cortisol levels** during the trial because BI 690517 could affect your blood cortisol levels. Your blood cortisol levels normally fluctuate daily, peaking in the morning and falling throughout the day. Your blood cortisol levels will be specifically measured in the early morning (ideally before 09:00) at two points in the trial: the one month and three month follow-up visits (and also if your local doctor requests it). Low cortisol levels can lead to vague non-specific symptoms and can cause fatigue, nausea, low blood pressure (so you may feel dizzy or light-headed) or low blood sugar. High cortisol levels can cause easy bruising, facial redness and stretch marks. If you notice any of these symptoms then please let your usual doctor and/or study team know.

Common everyday symptoms are often included in information medication inserts, and large trials help identify if new pills can increase their likelihood. BI 690517 is a relatively new treatment and so there may be additional side effects we are unaware of.

We will collect information on all possible side effects you experience for at least the first 12 months of the trial (whether the side effects are serious or not). Treatment information leaflets include a wide range of symptoms people might experience whilst taking any pill, and the trial will help us understand better any true side effects of BI 690517. This will include assessment of those currently listed including: cough, nausea (feeling sick), vomiting, diarrhoea or constipation, a fast or abnormal heart rate, difficulty sleeping, altered energy levels, muscle spasms, and back pain. These may not be true side effects, and the trial will help us understand BI 690517 better. For example, many of these symptoms may also happen if you are on the inactive dummy pill (placebo), as they are common in people being treated for a kidney problem or diabetes, and people who are older (ie over 75 years of age). Such groups of people may generally experience more side effects than other groups of people, but they may also have more to gain from any beneficial effects of treatments. EASi-KIDNEY will help identify if BI 690517 really causes all of these symptoms.

As with all medicines, some people can develop an allergic reaction, including itchy skin or a skin rash. Very rarely, some people may require emergency treatment for swelling around the mouth and throat causing difficulty in breathing which can even result in death.

Your doctor may also notice that your **kidney function slightly decreases**. This may actually be a sign of the protective effect of empagliflozin and BI 690517 (or perhaps just natural changes in your kidney function).

Throughout the study, the research team will carefully monitor you and your blood tests for possible side effects. Some side effects may mean that you need to stop taking your study pills temporarily or permanently.

The study research team will keep you up to date with any new important information we learn about the pills.

If you do experience unexpected symptoms and want to ask questions, you can contact your local study research team, or an EASi-KIDNEY study doctor based in Oxford, on Freephone 0808 1644060 or +44 (0)808 1644060 from outside the UK (available 24 hours a day, 7 days a week).

If new information is learnt about BI 690517 during the trial, we will share it with you in a new leaflet.

What are the other possible disadvantages of taking part?

No studies of empagliflozin or BI 690517 have been performed in pregnant or breastfeeding women or infants and it is possible that either medication could affect an unborn child. Women who are pregnant, plan to get pregnant or are breastfeeding cannot join the study. Women who could become pregnant must agree to use highly effective contraception[1] throughout the trial and for a week after the end of the study (types of contraception which are considered highly effective are listed below).

If you become pregnant during the trial (or wish to do so), you should stop taking your study pills and tell the local study team or study doctor promptly so appropriate action can be taken. Your local study doctor will keep in contact with you during and after your pregnancy to follow-up your pregnancy and collect monitoring information.

If you have private medical insurance or require travel insurance, your policy may be affected by joining the study, so please check with your insurance provider.

1 Highly effective methods of contraception include implants, injections, combined oral contraceptive pills (started at least three months before joining the trial), intrauterine devices (often known as a coil), vasectomised partner, or true and complete abstinence (ie not calendar or temperature methods).

What will happen at the end of the main part of the study?

The results will be published in health or scientific journals, on websites (including www.ClinicalTrials.gov), and will be discussed at major conferences. Others will learn from the results, which we hope will show that more lives can be saved by using empagliflozin and BI 690517. No individual participant will be identified in any report or publication.

We will try our best to inform participants and their GPs of the study results and any related publicity. We will use study newsletters and videos on the study website to inform people about what the study shows.

Your contribution to the study could be even more valuable if we have your permission to get information about your health after your very last study appointment. Therefore, we will ask for your permission to use your contact details, such as your email address, to continue to communicate with you after the study has ended. This way we can learn about any longer-term health effects of the study pills. This might include a questionnaire or phone call once a year, review of your medical notes, flagging with local registries or an interview with your local clinical team. For example, scientists can continue to get information about your health, such as details from your doctors, NHS England, the NHS Diabetic Eye Screening Programme (or other central NHS registry), and the UK Renal Registry.

Who is running the study?

EASi-KIDNEY will be coordinated by scientists from Oxford Population Health's Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU), part of the University of Oxford. CTSU is one of the world's leading centres for this type of research. More details of our team are available on our website: www.ctsu.ox.ac.uk/research/renal-studies-group. The Oxford team will be supported by many kidney doctors and other specialty doctors and nurses around the world, to make this 'megatrial' possible.

The EASi-KIDNEY team has permission from the relevant ethics committee to do the study (Oxfordshire Research Ethics Committee B, Ref No. 24/SC/0147). This committee has checked that the health question being asked is important enough to warrant a study, and that the study is being carried out in an independent, honest, and professional manner.

An independent committee of experts also watches over the study and keeps an eye on the safety of the participants. This committee could stop the study early if there was important new information from this, or other, studies which affected whether EASi-KIDNEY should continue.

If the study is stopped, the reason(s) for this and what the next steps are (including any adjustments to your management) will be explained by your study team following discussion with your local doctor.

Studies such as EASi-KIDNEY take a very large amount of collaborative effort from many hundreds of research staff around the world and can be costly to run. The study is sponsored by Boehringer Ingelheim, which

is also providing the study pills and a grant to the University of Oxford. Those running the study at the University of Oxford have also received support from the Medical Research Council and British Heart Foundation to run trials.

What if there is a problem during or after the study?

You have all the usual rights of an NHS patient if you join the study or not.

The University of Oxford has arrangements in place to provide for harm arising from participation in the study. In the unlikely event of you being harmed by taking part, insurance cover is provided by the study sponsor Boehringer Ingelheim International GmbH. Any compensation would be paid in accordance with the guidelines of the Association of the British Pharmaceutical Industry.

If you have a concern about any aspect of the study, you can speak with the EASi-KIDNEY team by calling a 24-hour Freephone number: 0808 1644060 (+44 1865 743868 from outside UK). If you remain unhappy about the study in other ways and wish to complain formally, you can do this through the NHS complaints system. You can get the details for the Patient Advice and Liaison Service (PALS) from your local hospital or online (https://www.nhs.uk/service-search/other-health-services/patient-advice-and-liaison-services-pals).

Thank you

Thank you for reading this leaflet. Our aim is to make your participation an interesting and worthwhile experience, while helping us and others to improve the treatment of people who have, or who are at risk of, kidney disease.

EASi-KIDNEY appointment schedule

	Questions about the pills and your health	Consent form	Physical measurements (e.g. blood pressure)	Blood sample	Urine sample	Randomization to BI 690517 or placebo	New supply of study pills provided
Screening visit	✓	✓	✓	✓	✓		✓
Randomization visit	✓		✓	✓	✓	✓	✓
Bloods only visit				✓			
First follow-up visit	✓		✓	✓			
Second follow-up visits	✓		✓	✓	✓		✓
Later follow-up visit	✓		✓	✓	(✓)†		✓
Final follow-up visit	✓		✓	✓	✓		

†Urine test and provision of saliva pots at 18-month visit only

EASi-KIDNEY participant documents

Prior to entry into the trial you will be required to read this **Participant Information Leaflet** and **Data Protection Information Leaflet** in order to enable you to be fully informed about the trial and complete the **Informed Consent Form** at your first Screening visit.

At your first Screening visit, in addition to a copy of the **Informed Consent Form** (if completed), you will be given the **Study Treatment Information Leaflet**, **Dietary Potassium Leaflet** and **Participant Card** which will provide important information for the duration of the trial.

Provided at Invitation:

1. **Participant Invitation Letter**: a letter providing a brief overview of this research study and inviting patients to participate
2. **Participant Information Leaflet**: this leaflet provides detailed information about this study to help patients decide whether they want to take part
3. **Data Protection Information Leaflet**: a leaflet explaining how data from EASi-KIDNEY are processed

Provided at Screening:

4. **Informed Consent Form**: a form to make sure each patient understands the main points about taking part in this research study and provides a record of consent to participate
5. **Study Treatment Information Leaflet**: a leaflet providing detailed information about the study pills (BI 690517 or matching placebo and empagliflozin)
6. **Dietary Potassium Leaflet**: a leaflet providing dietary advice for participants if they have a high blood potassium level
7. **Participant Card**: a card with contact details of the study team so that your clinical team can promptly report all hospitalisations and emergencies

Contact information

By telephone:

0808 164 4060 (24-hour freephone number)

+44 1865 743868 (from outside the UK)

By post:

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Website:

www.easikidney.org

Please contact the EASi-KIDNEY office if you would like to receive this document in another format

EASi-KIDNEY
Aldosterone Synthase inhibition & Empagliflozin in CKD

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