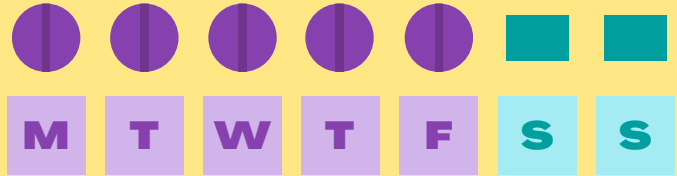


This is a Participant Information Sheet -for all participants (12-19 years) as well as their caregivers (as appropriate). Please read all the information, take your time and ask any questions you have.

**For caregivers:** where it says 'you' it is referring to 'your child'. This is because you are being asked to read this information on behalf of your child who is under 18 years old.

01

A clinical trial or study starts with a question.

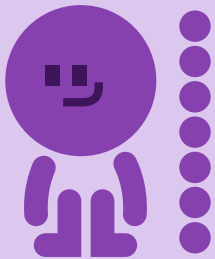


02

BREATHER+ is asking whether it is safe to take ART (HIV medicine) Monday to Friday, or Sunday to Thursday, and have weekends off.

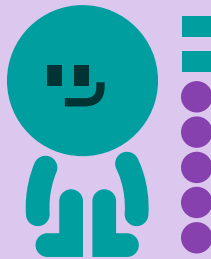
03

We will find this out by looking at two groups of people and watching them for 3-4 years.



**GROUP 01:**  
Continuous

Keep taking medicine every day.



**GROUP 02:**  
Short-cycle therapy (SCT)

Take medicine 5 days, then have 2 days off.



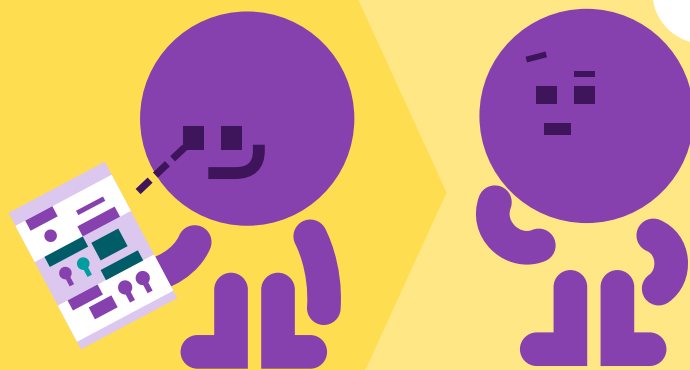
04

A computer decides which GROUP you are in. So you **MIGHT** just keep taking medicine everyday.

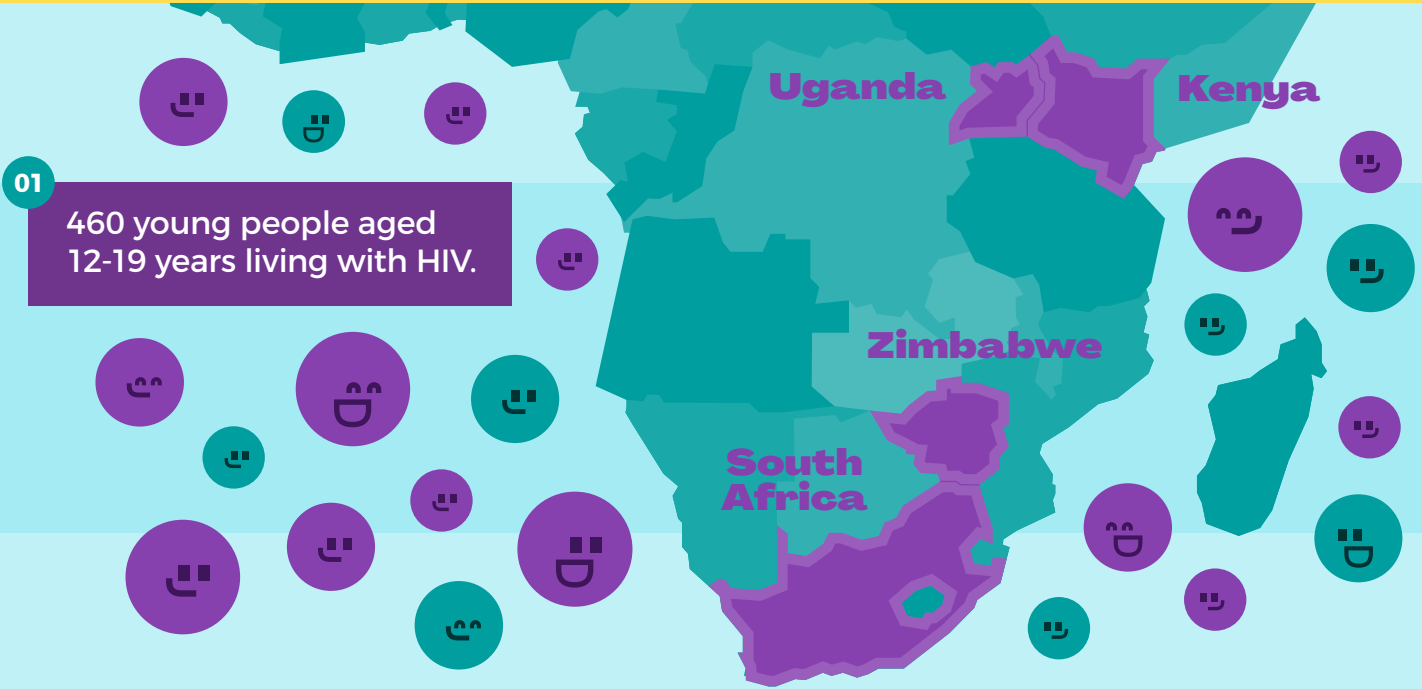
05

We need people to be part of this trial, so please read all the information and then...

**...YOU DECIDE!**



## WHO is going to be part of this trial?



## WHY is this trial happening?

02 Some of the HIV medicines now remain in the blood for a long time. We think you might be able to stop the medicine at the weekend but need to run this trial to check it is safe.



## WHY me?

03 There are lots of reasons:

- 1) You are interested in the research.
- 2) You know you have HIV.
- 3) You've been taking HIV medicine for over a year.
- 4) The medicines you are taking include dolutegravir, tenofovir and lamivudine/emtricitabine. You probably know this medicine as TLD (or sometimes as TED).
- 5) You are doing really well on medicine and have an undetectable viral load (which means the virus is completely asleep).
- 6) You are not pregnant – or planning to become pregnant during the trial – and if you are having sex, you are willing to use effective contraception (your clinic will help with this).

## Do I HAVE to?

No thanks!

No problem!



04 You can say 'NO' now, or leave the trial at any point. It will **NOT** affect the way you get your HIV medicine.

## If I say YES, what next?



01

- Aged 12-17? Give your permission by signing an **ASSENT** form. Your caregiver will need to give their permission too, by signing a **CONSENT** form.
- Aged 18-19? Give your permission by signing a **CONSENT** form.
- Have a blood test to make sure it is safe for you to join.
- Answer some questions about whether you are feeling happy or sad.

If you are female and have started your period:

- You will give a urine sample for a pregnancy test.
- The Doctor will talk to you about contraception. If you need this, it'll be free.

02

If you are in the SCT group, we see you after 4 weeks, then again after 4 weeks, to check you are OK

Week 1	Week 2	Week 3	Week 4
			✗
Week 5	Week 6	Week 7	Week 8
			✗
Week 9	Week 10	Week 11	Week 12
Week 13	Week 14	Week 15	Week 16
			✗

After this, **EVERYONE** comes to appointments every 8 weeks.

## BREATHER+ pilot group

The first 30 people who join we want to check really closely, so they will come every week for the first 4 weeks.

Week 1	Week 2	Week 3	Week 4
✗	✗	✗	✗
Week 5	Week 6	Week 7	Week 8
			✗
Week 9	Week 10	Week 11	Week 12
Week 13	Week 14	Week 15	Week 16
			✗

03

The HIV medicine will be provided to you for the BREATHER+ trial.



04

You give permission for Blood samples to be taken and stored up to 5 years after the end of BREATHER+.

## At each clinic visit: TESTS

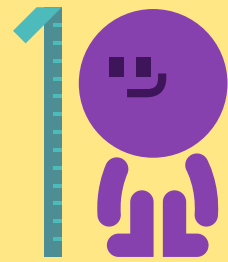
01

Blood tests to make sure the medicine is working properly (every 8 weeks in year 1, every 16 weeks in year 2 onwards), check your immune system, kidneys and liver (every year)



02

At some visits your height, weight, waist, blood pressure and pulse (to make sure your heart is healthy) will be measured. The Doctor will look for signs of any illnesses and ask you how you are doing.



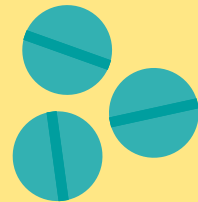
03

Check a urine sample to see if you are pregnant.



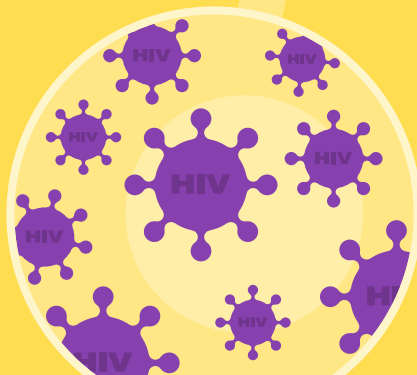
04

Check you are taking your contraception, if you need this.



05

Your clinic will test the HIV virus in your blood, usually once a year, but also if your Doctor has any concerns. If the level of HIV virus gets too high, you will need to come back for a second test at least one week later. If you are in the SCT group, and the second test is still the same, you will be asked to start taking your medicines every day for the rest of BREATHER+. You will not be able to have any more weekend breaks.



# At the clinic: You will be asked questions about...



BREATHER+

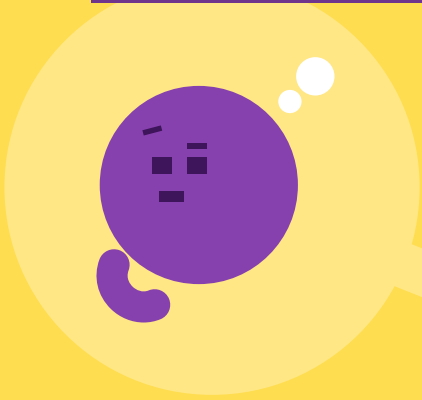
Patient Information Sheet

Master template 2.0 18-Mar-2020

05

01

How you feel about the trial and if you feel it is affecting your life.



02

How you are feeling.



03

How you are sleeping.



04

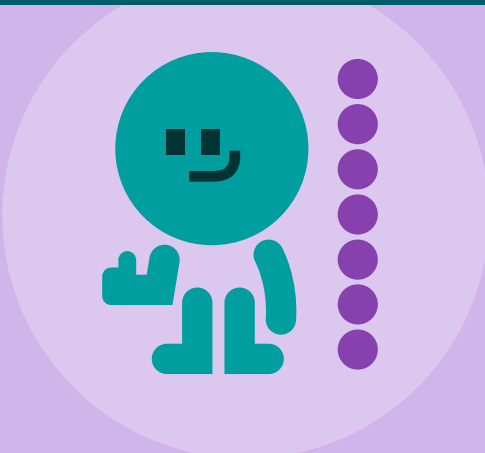
Taking the medicine - we want to make sure you are managing to take your medicine and if not, we can help and support you.



**At the end**

BREATHER + will last for 3-4 years.

You will then go back to your normal clinic, taking medicine **EVERY DAY**.

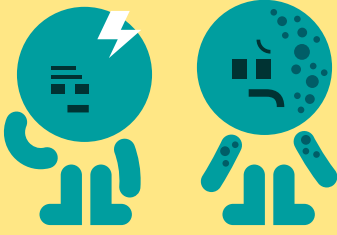


What we find out will help **ALL** children and young people around the world.

# Risks and side effects



We face risks everyday. This doesn't mean they are bad, we just need information to understand risks and then decide if we want to take them.



01

Sometimes the HIV medicine can cause a rash, itching, vomiting, stomach pain, weight gain, sleep problems, depression, lack of energy, feeling light-headed or may affect your liver, which is why the Doctor needs to watch you closely.

02

Very rarely, people on dolutegravir get very depressed, and have thoughts about suicide.



03



Very rarely women who were taking dolutegravir early on in pregnancy, have a baby with a damaged brain or not able to walk. This is called Neural Tube Defect. Although this risk is rare, it is the reason why it is so important not to get pregnant during the trial. See Additional Information.

Always tell your Doctor if you have side effects, feel sad, or just don't feel yourself anymore. They can help you with side effects.

## Advantages & disadvantages to taking part

### Advantages

- You are helping many other young people in the future.
- Making treatment better and easier to take for all young people living with HIV
- You might have freedom from your medicine at weekends.
- You may have fewer side effects.

### Disadvantages

- Come to the clinic more often.
- You might find it harder to remember to take your tablets if you are only taking them 5 days a week. Forgetting them can lead to more HIV virus in your body.
- The weekends off may not control the virus as well as taking medicines every day. This could mean your viral load goes up, and you have to change to different medicines to bring it down to undetectable.



It is important you take your time, and read all of this information. If there is anything you don't understand, ask your Doctor or nurse for more information. There is no problem if you don't want to do the trial. You will be looked after in the clinic just the same even if you decide not to take part in **BREATHER+**.

## Why this trial is called **BREATHER+**

This research trial is testing to see whether having a short 2-day break, or a 'breather' from your TLD HIV medicine, just at the weekend is as good as taking TLD every day.



## Confidentiality and your information

Your clinic has your contact details and keeps these confidentially, in a locked cabinet. If you join **BREATHER+**, you will be given a trial number and a 3-letter code. ALL study information, blood samples, and forms sent to the Researchers will be marked only with your trial number, 3-letter code and date of birth or year of birth. Your full name will never be used outside of the clinic.

### ■ What happens to your information

The Researchers need the information collected from you for the trial, and some information from your medical records, to be able to answer the question of whether having weekends off TLD HIV medicine is safe. This trial-related information will be sent to Researchers based in Africa, the United Kingdom and the Netherlands who designed this trial.

From time to time, the Researchers will ask for your clinic records to be checked against the information that has been sent to them. This is called monitoring. During **BREATHER+** 'Trial Monitors' will visit your clinic to check that the research is being done properly.

### ■ Your information after **BREATHER+** has finished

Once **BREATHER+** has finished, the Researchers will keep some of your information to check the trial results. They won't know who you are, no names will ever be mentioned in reports they write. They will keep your information for up to 25 years. All information in **BREATHER+** is kept safe and secure.

If you agree to take part, we would like your permission for Researchers to use the information and samples collected in **BREATHER+** for other HIV research.

### ■ Your information if you leave **BREATHER+** early

You can stop being part of **BREATHER+** at any time, without giving a reason, but please talk to your study Doctor or nurse first. They can help with any concerns you may have or provide you with more information.

If you decide to stop taking the study treatment, we would like to keep you in the trial and continue collecting information about you. This is important, because it helps us to make sure that the results of the study are reliable.

If you don't want to do this, that's fine, but we will keep the information and samples that we already have for you. To make sure **BREATHER+** runs properly, you would not be able to change any of the information/samples that have already been collected.

If you stop doing the trial early, it won't change your care at all, you will still be looked after and get your HIV medicines in the clinic.

### ■ Finding out more about how your information is used

You can find out more about how the Researchers use your information in the following ways:

- 1) Asking one of the research team. They can explain it to you.
- 2) Visiting this website: [www.ctu.mrc.ac.uk/privacy/](http://www.ctu.mrc.ac.uk/privacy/)
- 3) Sending an email to [data-protection@ucl.ac.uk](mailto:data-protection@ucl.ac.uk) with your questions about how your information is kept safe.
- 4) Visiting the Sponsor (UCL's) website: [www.ucl.ac.uk/legal-services/privacy/ucl-general-research-participant-privacy-notice](http://www.ucl.ac.uk/legal-services/privacy/ucl-general-research-participant-privacy-notice)



## Days off for the SCT group

If you are in the SCT group, your weekend off HIV medicines can be Friday and Saturday, or Saturday and Sunday. You can decide which is best for you.

## More information about what will happen at each clinic visit

You will have blood tests every 8 weeks in the first year in the trial. In year 2 onwards, blood tests will be every 16 weeks. At the yearly visit, you will have a blood test to check your immune system, blood sugar and levels of HIV virus. Every other year, blood tests will be done to measure your levels of fats, and see how you liver and kidneys are doing. Each visit will take 1-3 hours.

The usual amount of blood taken at each visit, is 1-3 teaspoons. But at 3 visits it will be 9-11 teaspoons because we need to do extra tests. The visits where more blood is taken are at the beginning of the trial, and at the beginning of every year after that while you are in the trial. This might sound like a lot of blood, but it is completely safe to take and you will feel fine.

At the very end of the trial, you will have a 'close-out' visit. At this last visit you will do some of the questionnaires and have a blood test to measure the level of HIV virus. Some of the blood from this test will also be stored for later analysis.

### ■ Blood tests you have to have

If you are part of BREATHER+ you will need to have blood tests to check how much virus you have in your body. Some of these samples we will store for up to 5 years after the end of the trial. As we said before, your name will not appear on any of these samples, they will be coded.

### ■ Tests you do not have to have

You will be asked if you are happy to have other blood and urine samples taken. These are optional, so you can say 'no'. These optional samples are taken and stored, and can be used later for research on HIV. They are done three times in the trial. We store these for up to 5 years after the end of the trial because new tests are being developed all the time. If your samples can be kept up to 5 years after the end of the trial, it will give us a better chance of using these new tests.

### ■ Travel costs for trial visits

Reasonable travel costs will be paid for all your trial visits. This will include costs for your carer's travel too (if you are 12-17 years of age).

### ■ Sending your blood tests to another country

Some of the stored blood tests may be sent to another country to be looked at in a laboratory. This is because the right kind of laboratory isn't always available in every country. These samples will not have your name on them, just your trial number, 3-letter code and year of birth.



## If your viral load increases

Your clinic will test the HIV virus in your blood, usually once a year, but also if your Doctor has any concerns. If the amount of HIV virus in your body gets too high, you will need to come back after about a week so we can test you again. If your test results are still too high:

### ■ SCT group:

You will need to start taking your medicine every day and stop having weekends off.  
**Your medical team will help you with this, so do not worry.**

### ■ Continuous group:

You might have to change your medicines to a different combination.  
**Your medical team will help you with this, so do not worry.**





## The medicine being used

The medicine in **BREATHER+** is called **T** (tenofovir), **L** (lamivudine), **D** (dolutegravir).

**TLD** is used very widely for the treatment of HIV and is a very safe medicine. It is a licensed HIV medicine. This means TLD has had lots of checks to make sure it works well to control the virus, and is safe to use. It is licensed for use in young people and adults. You will have already been on TLD for at least one month before agreeing to come into the trial, so this medicine isn't new for you.

Occasionally instead of TLD you might be on TED. In this combination, instead of lamivudine, there is another medicine called emtricitabine. This medicine works exactly like lamivudine, and is very safe and approved for use in children, adolescents and adults.



## Side-effects

All medicines have side effects and you must tell your Doctor or nurse if you feel anything different. This could be physical symptoms (rashes, feeling sick etc.) but also if you don't feel like your normal self.

### ■ Kidneys and bones

Two side-effects from this medicine that happen occasionally are that your kidney's don't function properly or that your bones aren't as strong as they should be. This is why we will be doing tests on these throughout **BREATHER+** to make sure you are OK.

### ■ If I get side-effects and have to change my medicines, can I continue on the weekends off?

You may have side-effects that means your Doctor thinks you should stop taking TLD. If this happens you won't be able to continue having weekends off. This is because other HIV medicine don't stay in the body as long as TLD. Because of this you will have to take your new HIV medicines every day. Your Doctor will give you more information about this.

### ■ Pregnancy

If you are female and accidentally get pregnant, there is a very small chance of your baby having something called 'Neural Tube Defect'. This is when the baby has a damaged brain or may not be able to walk. It is a small risk for every woman – about 1 baby for every 1000 pregnancies, but is a little greater if you take TLD in the first 8 weeks of pregnancy, about 3 babies for every 1000 pregnancies. Your Doctor will talk to you more about this.

If you decide you want to get pregnant then you must talk to your Doctor **BEFORE** this happens. The Doctor will talk to you about whether you stay on TLD or change to another medicine.

Also the Doctor will talk to you about taking folate. Folate is found in vegetables and other foods, it can also be taken as a tablet. All of us need folate, but it is very important early on in pregnancy. Folate reduces the risk of neural tube defect.

If you do get pregnant during the trial, then we want to make sure you and your baby are OK. To do this we will want to see your baby about a month after they are born, or get information from the clinic looking after your baby about how your baby is doing. This information will also be sent under a code to the pregnancy register in the United States. This pregnancy register is where information about the safety of HIV medicines in pregnancy is reported from all over the world. This information is really important for helping researchers to understand how safe HIV medicines are in pregnancy.

## Other things you should know

There is a very small risk from taking blood. People can feel dizzy, and sometimes there is pain when the needle enters through your skin. You can get a bruise or small blood clot where the blood has been taken. Very rarely, you can get an infection where the needle was inserted.

Continued on page 10



Your blood pressure will be measured using a band on your upper arm. The band tightens, and squeezes your arm for a few minutes. It can be a little uncomfortable but only for a minute or two.

Because one group of **BREATHER+**, the SCT group, will take HIV medicine 5 days a week and not 7, the virus may come back. If it does, then there is risk you could pass it on if you have sex without a condom.

## Sub-studies

Most clinical trials have 'sub-studies'. These are different small pieces of research that answer different questions from the main one the study is asking. In **BREATHER+** the sub-studies are:

### ■ Happiness

During **BREATHER+** you will be asked to fill in confidential questionnaires about:

- When you are taking your medication
- Whether you are happy with being part of the study
- Whether you have had any thoughts about harming yourself or even tried to hurt yourself, because you were very unhappy
- How it is affecting you and your life (in a good and bad way)

If these shows you are feeling unhappy, worried or having problems with sleeping, we may ask for you to speak with a specialist (a psychologist, or psychiatrist) to help you with how you are feeling.

We may also ask you to be involved in a 'neuropsychiatric sub-study'. There is a separate information sheet and assent/consent form for this.

Neuropsychiatric means looking at the brain and nervous system. This will help us understand why you are feeling the way you are and what is worrying you. It will also mean that we can help you.

We may also ask you to take part in this sub-study if you have none of these feelings, so we can check we are not missing anything else.

Being part of this sub-study means you will be asked to fill in different questionnaires. Your Doctor may also think it's a good idea to speak with a specialist (a psychologist, or psychiatrist) to help you with how you are feeling if the questionnaires in the sub-study suggest you are feeling very worried or unhappy.

### ■ Taking medicine (Adherence)

We need 200 young people from **BREATHER+** for another sub-study where they will use **MEMS** (Medication Event Monitoring Systems) caps.

A MEMS cap is an electronic device fixed to your medicine bottles which records when it is opened (the time and date). If you agree to take part in this sub-study you will be given a MEMS cap to fit to your medicine bottle for 6 months either in the first or second year of the trial. Your Doctor or nurse will explain how it works and show you how to use it.

### ■ How you are feeling

We want to find out more about how young people living with HIV feel about taking medicine, being part of this clinical trial and life with HIV. A few young people will be invited to be part of a sub-study run by Social Scientists. These are people specially trained to ask questions and really listen to your answers. If you want to be part of this, let your nurse or Doctor know. There is a separate information sheet and assent/consent form for this.



## When **BREATHER+** finishes

After **BREATHER+** has ended everyone will go back to taking HIV medicine every day. You and your Doctor will continue to make decisions about your treatment. If stopping HIV medicines at the weekend is found to be a safe and a good way of treating young people living with HIV you might be able to have a treatment break at weekends.



## How will you find out the results

When **BREATHER+** has finished, there will be some different ways to find out what was learnt:

- 1) We will tell all the participants, and their carers (as appropriate), the results. We may do this in a short information sheet, or through community meetings held at your clinic.
- 2) The Researchers will publish a summary of the results on the website of the MRC CTU at UCL [www.ctu.mrc.ac.uk](http://www.ctu.mrc.ac.uk)
- 3) The results will be published in a medical journal, so that other Doctors can see them and learn from them. You can ask your Doctor for a copy of any publication. Your identity and any personal details will be kept confidential. No named information about you will be published in any report of **BREATHER+**.



## Keeping you safe

**BREATHER+** has been looked at by an independent group of people called a 'Research Ethics Committee'. Their job is to check the study does not hurt anyone. They have said this study is safe.

A second group called the 'Independent Data Monitoring Committee' will meet regularly during the trial and decide if the trial should keep going or whether it is not safe and should stop.

## Where to report worries or concerns

If you have any concerns about the study, the way you have been treated in the trial or the way it has been run please talk to your study Doctor or nurse.

Investigators:

INSERT Investigator's names and phone number

The hospital running **BREATHER+**

INSERT Hospital name, Doctors' names and phone numbers

If you are still unhappy, or if you wish to complain, please use the normal clinic complaints process.

If you as the participant, are harmed by taking part in **BREATHER+**, or if you are harmed because of someone's negligence, then you may be able to take legal action. If this happens you can contact:

INSERT the details of the local REC

**BREATHER+** is funded by the European and Developing Countries Clinical Trials Partnership. This is a partnership between researchers in Europe and in Africa aimed at improving the health of people living in Africa.

**BREATHER+** is sponsored by University College London (UCL), which is a university based in the UK. This means UCL has overall responsibility for the conduct of the study.

## Questions?

Thank you for taking the time to think about being part of **BREATHER+**. Please ask any questions and let us know if there are things that you do not understand or would like more information about.

This information sheet has been developed by members of different Youth Trials Boards. These are groups of young people living with HIV who are working to give children and young people a voice in clinical trials and research. They represent different countries around the world.