ISRCTN Document Cover Page

EudraCT Number	2016-004633-24
Sponsor Protocol Number	CRUKD/17/009
Official Title	A Cancer Research UK Phase I/IIa Clinical Trial of BT1718, (A Bicycle Drug Conjugate) Given Intravenously in Patients With Advanced Solid Tumours.
Document, Version & Date	Patient Information Sheet and Consent Form – Expansion Phase, Version 11.0 dated 20 June 2022

The following different Patient Information Sheet and Consent Forms have been used for the CRUKD/17/009 Phase I/IIa clinical trial:

1. Patient Information Sheet and Consent Form – Pre-screening
2. Patient Information Sheet and Consent Form – Escalation Stage 1
3. Patient Information Sheet and Consent Form – Escalation Stage 2
4. Patient Information Sheet and Consent Form – Expansion Phase
5. Pregnancy informed consent document for the partner of a patient enrolled in the BT1718 clinical trial

The Patient Information Sheet and Consent Form for the Expansion Phase (4 in the list above) has been selected by the Sponsor (Cancer Research UK) as the most appropriate informed consent document to be made available publicly as this is the document that was most recently updated and used on the CRUKD/17/009 trial.

Please note: 'Bicycle Therapeutics Ltd' are referenced in this document as the company who make BT1718. The operations of Bicycle Therapeutics Ltd are now carried out by 'BicycleTx Limited'

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PATIENT INFORMATION SHEET AND CONSENT FORM

- Participation in a Phase I/IIa clinical trial

Expansion Phase

A Cancer Research UK Phase I Trial: A Cancer Research UK Phase I/IIa clinical trial solid tumours.

Short Title: A Phase I/IIa trial of BT1718 in patients with advanced solid tumours.

This information sheet has two sections:

- **Section 1** tells you about the purpose of this trial and what it will involve if you do decide to take part (e.g. tests, overnight stays).
- **Section 2** gives you more detail about how the trial is organised.

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Contents

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Section 1

1 Invitation

We would like to invite you to take part in this research study. Before you decide whether or not to take part, we want you to understand why the research is being done and what it would involve for you. Thank you for consenting for us to test your biopsy sample, to check if your cancer has a high level of a substance called 'membrane type 1 metalloproteinase' (MT1-MMP) which can make cancers grow more quickly. If you would still like to take part in the main clinical trial, we would need to perform some further tests before confirming if you can take part. This information sheet provides you with the information you need to have before making a decision and what will happen if you do go on to receive BT1718.

It is important that you take time to read this information sheet carefully. The study nurse or doctor will go through it with you. This information sheet contains information about the trial and an informed consent form at the end, which you will be asked to complete if you decide to take part. Reading the information sheet and talking to the nurse or doctor could take up to an hour. If you would like to, please feel free to talk to your family, friends and GP about the trial. Please take as much time as you need to decide whether or not to take part.

If you have life insurance, you should check if this will be affected by participating in this trial. Similarly, if you have private medical insurance, you should check with the company before agreeing to take part.

2 What is the purpose of the trial?

This clinical trial is looking at a drug called BT1718, a new anti-cancer drug which looked promising in laboratory studies. The trial started in 2018 and over 50 patients have received BT1718 across a range of doses. We now have a dose that we feel is safe and we now want to expand the trial and give this dose to more patients, who have high levels of MT1-MMP in their cancers. BT1718 was designed to recognise and attach itself to the MT1-MMP in cancer cells. Once attached, a piece of BT1718 is taken into the cancer cell which we hope will cause it to die.

This clinical trial has two parts: Part 1, in which we increased the dose of BT1718 so we could find the best dose to give, is now complete.

You are being invited to take part in **Part 2** of the trial where we are looking more closely to see if BT1718 works the way we think it should and are looking for about 70 patients with high levels of MT1-MMP in their cancer.

In this part of the trial we wish to find out:

- more about the potential side effects of BT1718 and how they can be treated;
- what happens to BT1718 inside the body;
- whether BT1718 can kill cancer cells, and how it does it.

This information will help us decide whether to continue testing BT1718 in future clinical trials.

3 Why have I been invited to take part in this study?

You have been invited to take part in this trial because you have a cancer known or expected to have high levels of MT1-MMP which may respond to BT1718. However, even though we have completed Part 1 of the trial, this is still the first clinical trial where BT1718 has been tested in people and we do not know if you will benefit from receiving BT1718. In this trial we want to recruit approximately 16 patients whose cancer has high levels of MT1-MMP into each of the two or three arms:

- One arm will include patients with lung cancer (**eight** patients in this arm will need to have **mandatory biopsies, see section 6(d)**.
- One arm will include patients with any type of cancer (all-comers arm) with high levels of MT1-MMP (**most** patients in this arm will need to have **mandatory biopsies, see section 6(d)**.
- Depending on what we see from these two arms, we may look at another arm for patients with oesophageal cancers.

Not all patients in Part 2 will have the same type of cancer, though all patients will have a cancer known or expected to have high levels of MT1-MMP. What arm of the trial you are in will depend on the type of cancer you have.

All patients will receive the same dose of BT1718 and all the tests are the same, but some patients will need to consent to having a biopsy performed (as mentioned above). Your doctor will explain this to you in more detail.

4 Do I have to take part?

It is your choice whether or not to take part. We will describe the trial and go through this information sheet with you and answer any questions you have. If you decide to take part, we will ask you to sign the consent form at the end of this document to show you have read and understood this information sheet and agreed to take part. We will need to perform other tests before we know you are eligible to take part. After all the tests are completed and the results known, there is a chance you may not be able to take part.

If you are eligible, **you are free to leave the clinical trial at any time and you do not have to give a reason.** The information we have already collected will be kept and used to help us understand more about BT1718 (see Section 15 and 24 for further details). If you decide not to take part, or you decide to leave the study, this will not affect the quality of care you receive.

5 What are the alternative treatments?

Your trial doctor will discuss other care options with you, including treatment for any symptoms you may have. There may be an opportunity to take part in other trials of experimental treatments. Your study doctor will explain the risks and benefits of other care options or treatments.

6 What will happen to me if I take part?

a) What tests do I need to have <u>before</u> I can take part in the clinical trial?

Because BT1718 has only been given to over 30 patients in Part 1, it is important to check that you are fit enough to receive BT1718.

Test done before you take part	Why do you need these tests?
Physical examination	To check your general health
Height, weight, temperature, pulse rate and seated blood pressure (vital signs)	We use your height and weight to calculate the dose of BT1718 you will receive
Electrocardiogram (ECG)	A heart trace to check your heart rhythm
Glomerular filtration rate (GFR) scan	A GFR scan may be required to make sure your kidneys are functioning well
Pregnancy test	Women able to have children will need to have a pregnancy test before receiving BT1718 to make sure they are not pregnant
Imaging – you will have one of the following imaging investigations (CT scan or MRI)	Computerised Tomography (CT) scan (a type of X-ray) that take images of your body and your cancer. A CT scan gives a more detailed picture than a single X-ray. It uses ionising radiation to take these pictures so there is a risk with any ionising radiation you are exposed to (see Section 11 for more information) **OR** Magnetic Resonance Imaging (MRI) scan - you may receive an MRI scan to take images of your cancer. MRI scans use magnets to make up an image of the scan area and do not use ionising radiation.
Routine blood tests	These are done during any treatment you would have for your cancer. These tests check on how well your kidneys and liver are working, whether your blood counts are low, and so on.
Research blood tests	These are taken only for this study. These will look at the amount of BT1718 in your blood, and how quickly it is removed.

Not all of these tests can be performed on the same day, so you may have to come to the hospital a few times. Some tests are done quickly (bloods, vital signs, ECG) but some can take a few hours (scans, GFR). Once you have had all these tests, we will be able to confirm whether or not you can take part in the trial. If you are not able to take part, your doctor will discuss other treatment options with you.

b) What will happen during the clinical trial?

You will need to attend the hospital **several times** in the first week you receive BT1718 so that we can monitor you for any side effects and take research blood samples. BT1718 is given as an intravenous infusion (a drip). Three drips (one every week) for three weeks with one week off is called a cycle. So BT1718 is given on Days 1, 8 and 15 (Weeks 1, 2 and 3) of each cycle. The other cycles are given in the same way.

In Cycle 1

Before and after you receive BT1718, research blood samples will be taken. Details of these blood samples are given in a table at the end of this information sheet.

The following will be performed during your visit in Week 1:

Day 1 (Week 1):

Physical examination	The study doctor will examine you before you receive BT1718.
Routine blood and urine samples	Routine blood sample will be taken before you receive BT1718. You will also be asked to give a routine urine sample.
Height and weight	Your height and weight will be checked to make sure it has not changed and we will use this to calculate the dose of BT1718 you receive.
Heart trace (ECG)	A heart trace will be performed **before and after** you receive BT1718.
Glucose finger prick test	Patients with diabetes will need to have a glucose finger-prick test performed **before and after** receiving BT1718. This is because BT1718 is added into a sugar solution so may increase blood sugar levels. If you are diabetic you may need to adjust what you eat or what medicine you take.
BT1718 infusion	You will receive BT1718, as an infusion (drip) lasting around **60 minutes.**
Blood pressure, pulse rate and temperature	Your blood pressure, pulse rate and temperature will be measured before, possibly during and after the infusion ends (45 to 75 minutes).
Research blood samples	Research blood samples will be taken in order to measure the levels of BT1718 in your blood. Approximately 90mL (6 tablespoons) will be taken over **two days** (at various times, which your doctor or nurse will explain to you). The timing of these samples may vary depending on what we see. You will have samples taken before you receive BT1718, part way through the infusion and at the end of the infusion. After the end of infusion sample, further samples will be taken on Day 2. This means you may need to **stay in hospital** so these samples can be taken, especially if you live some distance from the hospital. Your doctor may want you to **stay overnight** on Day 1 so we can watch out for any side-effects that may happen as a result of having BT1718. Your doctor will explain this to you.

Please note that there may be changes to the time points for taking research bloods as we receive new information about how the drug is working. However, your study doctor will discuss this with you if this is required. The total amount of research blood taken or visits will remain the same or may be less.

Day 8 and 15 (Weeks 2 & 3)

On Day 8 (Week 2) and Day 15 (Week 3) your doctor will examine you before you receive BT1718. A routine blood sample will be taken before you receive BT1718. Your blood pressure, pulse rate, temperature and glucose finger-prick test (diabetic patients only) will also be repeated. Research blood samples will be taken on Days 8 and 15 before you receive BT1718, please see Table 2 for details.

If you are having a biopsy (**see section (d) for more details**), one research blood sample will also be taken either **before or after** the biopsy procedure.

Week 4 (Day 22), Cycle 1 only

On Day 22 (Week 4), your doctor will examine you, a routine blood sample will be taken, you will be weighed, an ECG will be performed and you will also be asked to give a urine sample and a research blood sample. You will not receive any BT1718 this week. This should be a short visit.

Cycle 2 onwards:

You will continue to visit the hospital once a week for three weeks (Days 1, 8 and 15) to receive BT1718, followed by one week off, you may need to come into hospital between visits if your doctor thinks this is needed, but they will discuss this with you. At each of your clinic visits your doctor may briefly examine you and will assess whether you should continue to receive BT1718.

At these regular visits, you will have the following before receiving BT1718:

Side effects check	Your doctor or nurse will ask you about any side-effects you have experienced and ask you to tell them about any medications you have taken since your last visit.
Routine blood and urine sample	A repeat of the routine blood and urine tests
Research blood sample	We still need to take some research blood samples to check how BT1718 is working in your body. These samples will be taken **before, during and after** you receive BT1718 from Cycle 2 onwards (e.g. Cycle 4 Day 1, Cycle 6 Day 1). See Table 2 at the end of this document (before the consent form) for more details.
Research biopsy and blood samples	If you have agreed to have a biopsy taken (for some patients this will be mandatory, so you will have to agree to this to take part in the trial), please see Section (d) for further details. A research blood sample will also be taken either **before or after** the biopsy has been taken.
Blood pressure, pulse rate and temperature	Your blood pressure, pulse rate and temperature will also be repeated.
Glucose finger prick test	Glucose finger-prick test **(diabetic patients only)** will be repeated during Cycle 2. After Cycle 2 further tests will only be repeated if your doctor thinks it is necessary.
Heart trace (ECG)	From Cycle 2 onwards a heart trace will be repeated before and after BT1718 on Day 1 only of every second cycle (i.e. Cycle 4 Day 1, Cycle 6 Day 1 etc.).

Scans at the end of every 2 cycles to assess disease response

At the end of every 2 cycles (about every 56 days or 8 weeks) you will have a repeat CT or MRI scan, (depending on which one you had before your first dose of BT1718) to assess your cancer. If the scan shows that your cancer is growing then you will stop receiving BT1718. Your doctor will discuss your treatment options with you and will arrange for your care to continue.

If the scans shows the cancer is stable or reducing in size, you will be able to carry on receiving BT1718 (as long as you are not experiencing any side-effects caused by BT1718 that would mean it is better to stop receiving it) if you still want to for up to two years while the trial is still recruiting. You are free to withdraw from the clinical trial at any time without giving a reason. If you decide to withdraw from the study, any information we have already collected will be kept as part of the study.

c) What happens after I stop BT1718?

Within four weeks after your last dose of BT1718, you will need to visit the hospital for a check-up, including measuring your temperature, blood pressure, heart rate, blood and urine tests, and possibly a further CT or MRI scan, if you have not had one recently. This is called your 'off-study' visit. If you experienced any side effects considered to be related to BT1718, that are still ongoing at this visit, we will continue to monitor these at least monthly until they stop, or you start another anti-cancer treatment. You will be followed by your doctor in clinic as normal so there are no special visits needed. One larger research sample of blood will be taken and split into four samples at your off-study visit. Please see Table 2 for full details.

We will also collect regular information on your disease status until the end of trial; this may be checked every three months by your study nurse or doctor via the NHS electronic data records or during clinic appointments, or by telephone, if appropriate.

d) What other tests may I have?

Research Biopsy samples

If your cancer is the type that fits into what we call the **all-comers arm** (where there may be lots of different types of cancer), this biopsy **is mandatory** for most patients. If this applies to you, you **will not** be able to take part in the trial if you **do not** agree to have the biopsies performed.

For the other arms of the trial (patients with **lung or oesophageal cancer**), not all patients will need to have a biopsy performed, but we do need at **least eight** (half the required number of patients per arm) patients to agree to biopsies. If we have already recruited patients into these arms of the trial who have not had a biopsy (all patients will be asked) and this is when you have been approached to take part, you **will not** be able to take part in the trial if you **do not** agree to have the biopsies performed.

The biopsies are an important part of the trial, the answers we hope to get when the sample is analysed in the lab will tell us so much about BT1718, so please read this section carefully, and ask the doctor if you have any questions.

- **Why are biopsies being performed?**

We are taking biopsies to see how BT1718 is working and whether we can predict which patients may respond to it. We will look at the levels of MT1-MMP in your cancer, as well as substances that show how BT1718 is working. You will not get any direct benefit from this, but this information will help us learn more about the drug and whether certain people will benefit more than others.

- **How will the biopsies be taken?**

There are lots of different ways to have a biopsy taken and for this trial we would also like to take what is called a 'skin punch biopsy' as well as a more traditional biopsy (please see information at the end of this section).

A biopsy is the removal of a small piece of tissue. This is **usually** by passing a needle from the outside of the body to an area of cancer near the surface. Depending on the best area to take the biopsy from, sometimes it is necessary to take the biopsy while you are having a scan so that the person taking the biopsy can clearly see the best location to take it from. You are usually awake while you have the biopsy but you will be given a local anaesthetic beforehand to numb the area. However, it may still be painful or a little uncomfortable afterwards. Please tell your doctor if you have any pain.

The biopsy site may have some stitches that need to be removed after a few days. Your study doctor or nurse will do this for you and they will cover the area with either a sticky plaster or a gauze pad. There may be a small amount of bleeding which is perfectly normal, but the doctor or nurse will make sure this has stopped before you go home. If the biopsy site does start to bleed again, press on the area with a clean cloth or handkerchief. By pressing on the area, this will help your blood to clot and the bleeding to stop. If the bleeding does not stop or you feel pain, please contact your doctor. This covers the common type of biopsy that is performed but not all cancers can be biopsied in this way.

Depending on the type of cancer you have and where it is in your body, the biopsy procedure may be different.

Lung cancer

If you have **lung cancer**, a biopsy sample may be taken through a bronchoscope (e.g. if your lung cancer was also originally diagnosed with a bronchoscope and this was still felt to be the best way to get a biopsy). This is where a doctor will insert a bronchoscope (a flexible tube of about half a centimetre diameter) up through your nose and into your windpipe (bronchus). The tube is then passed into your lungs so that the doctor performing the bronchoscopy can have a look inside your lungs. To make this more comfortable for you, your doctor will spray the back of your throat to make it numb and you will have this done under mild sedation (medicine to make you drowsy) rather than under a general anaesthetic. The tube enters through your nostril and goes down the back of your throat, this can make you gag, but the spray will help. Once in the lung your doctor will be able to take samples of your cancer. The procedure usually takes a few minutes but can take longer and can be done as an outpatient. You will need to stay at the hospital for about an hour after the bronchoscopy to make sure you have recovered from the sedation and that you are able to swallow normally. Your nostril and the back of your throat may be a little sore afterwards but this should pass quickly. You will not be able to drive for the rest of that day so may need to attend hospital by ambulance or with family or friends who can bring you in. As with any surgical procedure there is a risk of bleeding, perforation (making a hole) in the windpipe or lung, or developing an infection. Your doctor will ask you to sign a hospital consent form after explaining these risks to you. This is in addition to you agreeing to the biopsies on the consent form at the end of this document.

Oesophageal cancer

A similar procedure may be used for patients with **oesophageal cancer**. Before you have this you will be asked not to eat or drink for about eight hours before the procedure, your doctor will give you full details. This time the tube is called an endoscope because it goes into the gullet (oesophagus) and sometimes into your stomach. The tube is usually inserted through your mouth so there is a rigid plastic mouth piece inserted first so you cannot bite down on the tube. It can make you gag, but sedation will help. Sedation is not always used, some patients prefer not to have sedation, this will be your choice. Sometimes an anaesthetic spray is all that is

needed to numb the area at the back of your mouth and throat. You may be asked to lie down for this procedure.

Once the endoscope is in the right place, the doctor can take a biopsy of any cancer they see before the tube is removed. You can have a sore throat afterwards because of the tube being inserted, but it is thin and flexible so should not cause much pain afterward. If you have had sedation, then the nurse or doctor will make sure you can swallow properly before you have anything to eat or drink. Once this is confirmed, drinking will help with the sore throat.

Normally an endoscopy of this type takes about 15-20 minutes and is performed in a small theatre. You normally stay in the recovery area for up to an hour afterwards before you will be allowed to go home. It is best that you do not drive after this procedure, so we can either arrange an ambulance or ask a member of your family or friend to bring you and take you home. As with any endoscopy there is a small risk of bleeding or perforating (going through the wall) the gullet or stomach, as well as infection. Your doctor will ask you to sign a hospital consent form after explaining these risks to you. This is in addition to you agreeing to the biopsies on the consent form at the end of this document.

If you want more information about any type of biopsy and what will happen, please ask your doctor or nurse.

- **When will the biopsies be performed?**

If you agree to the biopsies, a traditional biopsy will be taken **before** you receive your first dose of BT1718, and one will be taken **after** BT1718. If you have recently provided a new biopsy sample to check whether you are suitable for the trial, you will not need to provide another biopsy sample before BT1718.

The second biopsy will be taken during Cycle 1, this is likely to be on Day 8 or Day 15 (or up to 3 days after you receive BT1718). If the sample cannot be taken during Cycle 1, this can be done during Cycle 2, on Day 8 or Day 15 (or up to 3 days after you receive BT1718). Due to the timing of the biopsy, if the biopsy cannot be performed on the same day you receive BT1718 you may need to stay overnight or come back the next day or another day. Your study nurse or doctor will explain this to you.

- **Non-tumour Biopsy samples (Optional)**

If you consent to have the biopsies taken, your trial doctor will also ask you to consent to have a biopsy sample taken from an area where you do not have any cancer (non-tumour biopsy). This is to see whether BT1718 makes any changes to normal cells of your body.

If you consent to us taking non-cancer biopsies then we will remove a small piece of normal tissue close to the cancer site at the same time you have a biopsy of your cancer taken. If you are willing to have this done, please agree to this on the consent form at the end of this document.

If you are not happy to consent to these non-tumour biopsies, you will still be able to take part in the trial.

- **Skin punch biopsy research sample (Optional)**

For a skin punch biopsy a sample of skin and a bit of the fat beneath is taken using a punch biopsy needle. The needle looks a bit like a syringe and has a plunger. The area where the biopsy is to be taken is numbed with either a cream or a local anaesthetic and the doctor taking the biopsy will place the nose of the needle against your skin and press the plunger. The cutter

or needles in the syringe then form a circle as they enter and when the plunger is released, the biopsy sample is taken with it. This is then sent to the laboratory.

Stitches are not normally needed and a small dressing is applied. The area may be sore for a few days afterwards but once healed it just looks like a small dimple. Your doctor will explain this in more detail.

If you agree to the skin punch biopsy, this will be taken usually during Cycle 1 on Day 8 or 15, but if this is not possible this can be done during Cycle 2 on Day 8 or 15. The biopsy will be performed after your dose of BT1718 on the day agreed.

If you agree to have the skin punch biopsy, and if you are having the traditional biopsy as well, this would be done at the same time.

If you are not happy to consent to these skin biopsies, you will still be able to take part in the study.

- **What will happen to my samples?**

The samples will be sent to a laboratory and analysed. Once all the research tests have been performed, anything left from the biopsies will be considered as a 'gift' and may be used for other research tests related to BT1718 or other ethically approved research that is not related to BT1718.

Research blood samples and tumour biopsy for genetic (DNA) analysis

As part of this clinical trial, we will take extra samples of blood before you receive your first dose of BT1718 on Cycle 1 Day 1, 8 and 15. This sample is for a test called 'Genotyping' which allows us to look at genes which control the cells in our body. Genes tell your cells how to produce proteins that make up the structure of your cells and tell the cells how to behave. They are what controls what our hair or eye colour may be and are passed to us from both parents. This test may tell us why BT1718 helps some people more than others.

We may also look at your tumour biopsy if you have had one (see Biopsy Samples section above for more information).

The results of the genotyping tests are used for research purposes only and the results will not affect your health or medical care. All results will be kept confidential and your name will not be used. You will not be provided with the results of this test.

Due to the nature of this clinical trial, if you are not happy to consent to the genotyping sampling, you will not be able to take part in the trial.

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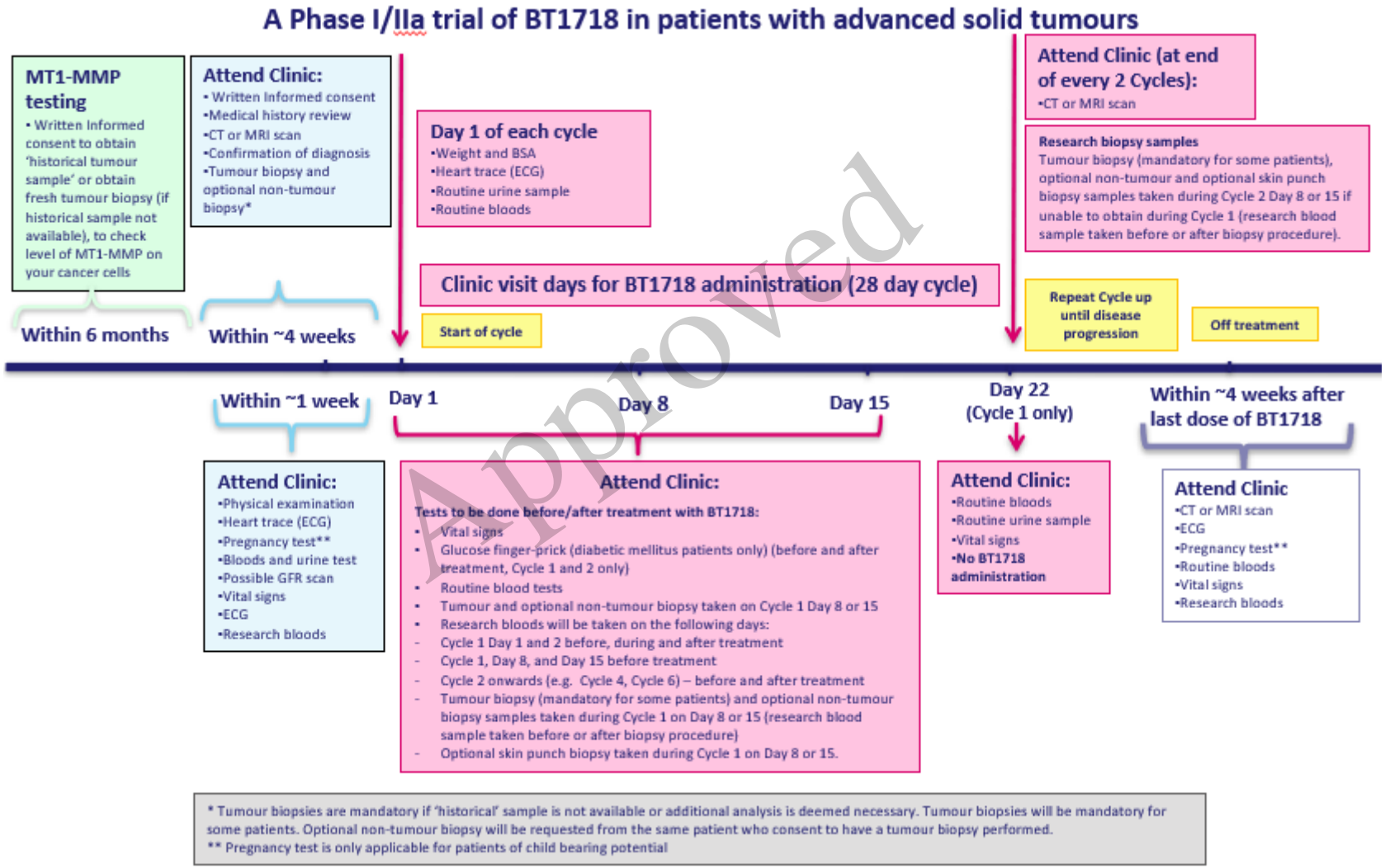
Table 1 Schedule of Events



7 Trial Design

This is what we call an open-label trial because all patients receive BT1718. We have already discussed the trial in detail with you and you have been asked to take part because now we wish to see if BT1718 can benefit patients with your type of cancer.

8 Expenses

We will need to see you at the hospital for tests before you receive BT1718 to make sure you are eligible. If you are eligible we will see you once a week, for three weeks, followed by one week off (three times per month) except on the first cycle where we will ask you to come to the hospital on your rest week. If you need to come in for extra visits, we will explain this to you. This is more than you would have normally visited the hospital but this is so we can closely watch the effects of BT1718 and manage any side effects you may experience.

You will have approximately nine visits in total for the first two months. Your study nurse will provide you with your appointment dates and times when you will need to attend. Reasonable travel expenses and hotel stays for trial visits can be reimbursed, including parking at the hospital and refreshments for you and if you come with a friend or family member, you can claim refreshments for them too, but you will need to keep any receipts. Any claims will be paid for by the hospital, but these will be reimbursed by Cancer Research UK who are sponsoring (running and funding) this clinical trial.

9 What do you have to do?

Everyday activities

You need to give a certain degree of commitment when you take part in a study. For example, you will receive BT1718 three times per cycle (one month) and you may need to visit the hospital more often, or have extra tests. You may also need to spend **long days** in hospital when receiving BT1718 (for example early in the morning to late in the evening).

You may need to stay in hospital or local hotel overnight on occasions so we can closely watch the effects of BT1718 and manage any side effects you may experience. Section 6 in this information sheet explains what you will need to do if you take part in the trial.

Sun exposure

We don't yet know whether BT1718 could cause side effects to the skin that could be brought on by exposure to sunlight. Your doctor will talk to you about your lifestyle and how much outdoors activity you undertake and will give you appropriate advice about protecting yourself from direct sunlight whilst you are receiving the study drug. While receiving the study drug you should avoid excessive sun exposure when outdoors during the daytime. Wear protective clothing, including a hat and sunglasses (where appropriate), and use protective sun cream with a high sun protection factor (SPF) of 30 or above (SPF30). Sun cream should also be used for one week after you have stopped receiving the study drug. You should also avoid sun beds during this time.

Diet

There are no specific restrictions on what you can eat or drink. If you do have a bronchoscopy or endoscopy as part of taking a biopsy, your doctor will discuss what you can eat or drink beforehand.

Other medications

While you are taking part in this trial you should let your study nurse or doctor know of any medication you are taking, including any herbal or vitamin supplements or drugs bought 'over the counter' at chemists and supermarkets.

If you decide to take part, we will give you a small card that shows you are taking part in this clinical trial. While you are participating in the trial, you should carry this card with you at all times and show it to other doctors, nurses and other health professionals such as dentists and opticians that may be involved in your care outside of this trial.

10 What are the possible side effects of any treatment received when taking part?

Like all drugs, BT1718 has side effects, but not everyone gets them. Only just over 30 people have received BT1718, we don't know all of the possible side-effects. As we go through the trial, we may have more information about possible side effects, which your doctor will share with you. You may also be asked to sign an updated consent form.

The trial doctor will examine you regularly, and blood tests will be taken to check for side effects. If you feel unwell or in any way different from usual while receiving BT1718, please let your nurse or doctor know as soon as possible.

Based on laboratory studies and what we have seen in Part 1 of the trial, these are the side effects we know may occur:

Possible side effects	How will the side effects be managed
Number of platelets, white blood cells and red blood cells are expected to either decrease or increase	The number of platelets (the cells in your blood that help it to clot if you cut yourself), white blood cells (the cells that help you fight infections) and red blood cells (the cells that carry oxygen around your body) are expected to change It is important that you let the study doctor or nurse know if you are feeling unwell in any way as they can give you treatments such as antibiotics or other medicines if necessary. Low counts of any of these cells can mean it takes longer for any bleeding to stop, an infection may take longer to clear (and you might need antibiotics) or you may feel more breathless or become anaemic and require a blood transfusion. Changes in blood cells have different effects and, even if you don't experience any symptoms, we will continue to monitor you to help prevent future problems. Your doctor may decide to take additional routine blood samples to monitor any of these side effects. This may mean extra visits to the hospital.

Possible side effects	How will the side effects be managed
Local injection site reaction	If BT1718 leaks outside the vein into the skin, fat and tissues surrounding the cannula (the small plastic tube inserted into a vein which connects to the drip) then this may cause pain or swelling. If you feel any pain during the infusion please let the study nurses know straight away as they may need to stop the infusion. If this happens, the study nurse will explain what will happen next. At the moment, we do not believe that if BT1718 gets into the tissue it will cause any long-term effects.
Liver changes	The liver is the body's filter and many drugs are processed through the liver. Any changes to how your liver is working will be picked up by routine blood tests.
Kidney changes	Most drugs are removed from your body through your urine. Routine blood samples will monitor your kidney function to make sure they are working properly. It is important that you keep drinking fluids while receiving BT1718 as this will help the kidneys flush the drug out of your system.
Neurological changes	BT1718 may also cause neurological changes (usually reversible after stopping BT1718). These changes can be mild such as a runny nose, pins and needles in hands and feet, up to loss of sensation or a spongy feeling in the hand and feet or other parts of the body. Other types of changes may also occur such as weakness in arms and legs. You should let your doctor know if you have any of these symptoms.
Gastrointestinal (gut) changes	Nausea and vomiting is common with a lot of anti-cancer treatments, it is possible that these may occur and your study doctor or nurse will provide you with anti-sickness medicines if necessary. Diarrhoea is also a possibility and medication can be prescribed. Should any of these symptoms become problematic it may be necessary to reduce, delay or stop BT1718 for a short time or permanently. Please let your study doctor or nurse know if you experience any symptoms.
Adrenal changes	Your adrenal glands produce hormones that control your blood sugar levels, blood pressure and so on and sit above the kidneys. BT1718 may cause your blood pressure to be either high or low which can mean you feel dizzy or have a headache as well as other symptoms.

Possible side effects	How will the side effects be managed
Salivary gland changes	You may also experience a dry mouth. You will be monitored closely at each clinic visit and may need to use a special artificial saliva to stop your mouth drying out too much. It is important to keep your mouth clean and brush your teeth regularly as well as drinking plenty of water.
Fatigue (tiredness, low energy)	A lot of the side-effects listed can make you feel more fatigued (tired) than usual. Just coming into hospital can be tiring. We do also think that fatigue may be linked to BT1718 (a lot of cancer drugs can make you feel this way), although not every patient has experienced this. Fatigue can be mild but it can also be severe and energy levels can become so low that it may make you feel like you cannot be bothered to do anything. It is important to try and keep to a normal routine and eat regular meals to keep your energy levels up, but if you need to rest then you should rest. You must let us know if this is becoming a problem for you as there may be something we can give you to help with these symptoms.

As BT1718 is a new drug there may be unexpected side effects in addition to those listed above.

Depending on the side effect you experience it may also be necessary to reduce the dose of BT1718 you are receiving, delay or stop BT1718 for a short time or permanently. Your doctor will explain this to you, if this were to happen.

If you take part in the study, you must report any medical problems you have to your trial doctor. There is also a contact number given at the end of Section 2 (see Section 27) of this information sheet for you to phone if you become worried at any time.

11 What are the other possible disadvantages and risks of taking part?

As mentioned in Section 1, if you have any private medical insurance or life insurance, you should check with them to make sure taking part in a clinical trial does not invalidate the cover. In Section 10, we mention that this trial requires a lot of time spent visiting hospital, you may even need to visit the hospital more often, or have extra tests and you may need to stay in hospital overnight on at least one occasion so we can closely watch for any effects of BT1718 and manage any side-effects you may experience. We appreciate that this may impact on your normal day-to-day life, but it is important to make sure you are not experiencing any side effects and to further our understanding of how BT1718 works.

a) Ionising Radiation (Medical Exposure) Regulations - IRMER

In order to find out if BT1718 is working you will have an initial CT and/or MRI scan before you start Cycle 1 (this may have been performed at the end of your previous treatment, and if it was within 28 days of you taking part in this trial then we will not repeat it just for this trial) and additional CT and/or MRI scans throughout the time you are taking part. If you agree to tumour

biopsies you may also require a CT scan or Ultrasound to help guide the doctors to the best place to take the biopsy from (See Section 6(d)). During screening you may also be required to have a GFR test to look at your kidney function.

CT scans expose you to radiation in the form of x-rays. A GFR test will involve an injection of a radioactive liquid into a vein followed by up to 4 blood tests spaced out on the same day.

MRI scans do not expose you to radiation.

The total amount of radiation you will receive will depend on how long you stay on the trial (i.e. how many CT scans you receive and biopsies you have that require a scan).

Exposure to radiation carries risks of developing cancer, the risk from the CT scans, CT-guided biopsies and GFR test also carries with it the same risk that it might cause another cancer sometime later in life. Exposure to radiation at the typical doses used for scanning and investigations would not normally cause cancer immediately. This may be something that develops over a long period of time (if at all) and this is called the latency period. This delay can be from 2-10 years for leukaemia, and up to several decades for other cancers. The risk to a healthy 40-year-old from the maximum total radiation exposure involved in this study is estimated to be approximately 1 in 65 (1.5%), a small increase on the lifetime risk of having a fatal cancer of about 1 in 4 (25%); the actual radiological risk to subjects with your pre-existing clinical condition will be much lower

b) Harm to the unborn child

The effects of BT1718 on the female eggs, male sperm and unborn child are unknown. If you are a woman and there is a chance you could get pregnant or you are a man and could father a child, please read the rest of this section. If this does not apply to you, please go straight to the next section (Section 12).

For women:

Please share this information with your partner if it is appropriate. BT1718 might harm the unborn child. You cannot take part in the study if you are pregnant or breast feeding. You should not take part in the trial if you intend to become pregnant during the trial or for six months after your last dose of BT1718. If applicable, you will be asked to have a pregnancy test before taking part. If you do decide to take part in the study and you are a woman and there is a chance you could get pregnant, then you must use appropriate medically approved contraception, such as:

- oral contraceptives and condom
- intra-uterine device (IUD) and condom
- diaphragms with spermicidal gel and condom

You should use these contraceptives for 4 weeks before you join the study, throughout the study and for six months after your last dose of BT1718.

If you do become pregnant while receiving BT1718 or within six months of your last dose of BT1718 you must tell your study doctor **immediately** so you can discuss your options. Your study doctor will discuss with you the possible risks to your unborn baby and they will offer you arrangements to monitor the health of both yourself and your unborn baby. You will be invited to sign a consent form allowing your study doctor to provide Cancer Research UK (the Charity who are running this trial) with confidential information on how your pregnancy progresses, and your health and the health of your child. Cancer Research UK may wish to have more information about your baby from time to time, but this will be discussed with you if necessary.

If you have any questions about this, please ask the study nurse or doctor.

For men:

Please share this information with your partner if it is appropriate.

It is not known if BT1718 will affect sperm or semen but there may be a risk of irreversible infertility. If you are concerned by the risk of possible infertility, please discuss this with your doctor who will discuss options with you which may include sperm banking.

BT1718 may affect the sperm or semen in ways that do not lead to infertility, but could cause problems for any children. Therefore, you must not father a child while receiving BT1718 or for six months after your last dose of BT1718. You and your partner must use reliable forms of contraception during this period, such as:

- oral contraceptives and condom
- intra-uterine device (IUD) and condom
- diaphragms with spermicidal gel and condom

If your partner is pregnant or breast-feeding when you enter the trial, you should use barrier method contraception (condom plus spermicidal gel) to prevent the unborn baby or the baby being exposed to BT1718.

If your partner does become pregnant whilst you are receiving BT1718 or within six months of your last dose of BT1718 you must tell your study doctor **immediately** so you and your partner can discuss your options. Your study doctor will discuss with you the possible risks to your unborn baby and they will offer you arrangements to monitor the health of your partner and your unborn baby. Your partner will be invited to sign a consent form allowing your study doctor to provide Cancer Research UK with confidential information on the pregnancy and birth of your child.

If you have any questions about this please ask the study nurse or doctor.

12 What are the possible benefits of taking part?

This trial aims to find out information that may help people with cancer. There may be some benefit to you but this is unknown at this stage.

13 What happens when the trial stops?

Once we have recruited the required number of patients for Part 2 of this trial, the trial will be closed to recruitment, but there may be patients still receiving BT1718. If your study doctor and Cancer Research UK think you are benefiting from receiving BT1718 you will continue to receive it for up to two years as long as there is sufficient BT1718 available.

When you are no longer receiving BT1718, your study doctor will arrange for your medical care to continue, and you will have regular appointments to see a doctor as usual.

The authorities who approved the trial will be told it is closed and Cancer Research UK will write up the results of the trial. The results will be published on the Cancer Research UK website at the link below. Your trial doctor will be able to provide you with a copy if you do not have internet access.

The website can be found here: http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-bt1718-for-advanced-cancer

14 What if there is a problem?

If you have any concerns about the way you have been treated during the trial or you are worried about possible harm you might suffer, you should discuss this with us. There is detailed information about this in Part 2 of this information sheet.

15 Will my participation in this study be kept confidential?

Yes. All the information about your participation in this study will be kept confidential. The details are included in Part 2.

16 Further Guidance

CancerHelp is the patient information website of Cancer Research UK. The website provides a free information service about cancer and cancer care for patients with cancer and their families: http://www.cancerhelp.org.uk

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Section 2 of A Phase I/IIa trial of BT1718 in patients with advanced solid tumours

17 What if relevant new information becomes available about BT1718?

Sometimes during the course of a clinical trial, we learn important new information about side effects (safety information) and general effects of BT1718. If this happens, we will tell you about it and discuss with you whether you want to continue in the trial. If you decide to stop taking part we will make arrangements for your care to continue. If you decide to continue in the trial you may be asked to sign an updated consent form.

On receiving new information, we might consider it to be in your best interests to withdraw you from the trial. If so, we will explain the reasons and arrange for your care to continue.

18 What will happen if you don't want to carry on with the trial?

If you decide to leave the trial we will keep the information we have collected up to the point you withdraw. If you are experiencing any side effects we would like to continue to collect this information and with your consent we may need to do further tests. Unless you refuse for this to happen, we will continue to collect the information.

The doctors will keep any research blood or biopsy samples you have given for the trial and they will examine these. But as with all your information it will be kept confidential and your name will not be used.

19 What if there is a problem?

Complaints:

If you have a concern about any aspect of this trial, you should ask to speak to the study doctor. They will do their best to answer your questions (contact number is given at the end of Part 2 in Section 27). If you are still unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

NHS Trusts are responsible for clinical negligence and other negligent harm to individuals that are under their duty of care.

Harm:

Compensation for any serious injury caused by taking part in this trial will be in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). Copies of these guidelines are available on request.

ABPI guidelines in Summary:

- Broadly speaking, the ABPI guidelines recommend that "the sponsor", without legal commitment, should compensate you providing you can show, on balance, the injury arose from your participation in the study without you having to prove that the sponsor is at fault. This applies in cases where it is likely that such injury results from giving any new BT1718 or any other procedure carried out in accordance with the protocol for the study.

- The sponsor of this study is Cancer Research UK and it will arrange compensation in accordance with the ABPI guidelines. Cancer Research UK will not arrange compensation

for you where such injury results from any procedure carried out which is not in accordance with the protocol for the study or the injury is caused by the negligence of a third party (including a doctor's failure to deal adequately with a side effect).

- Your right at law to claim compensation for injury where you can prove negligence is not prevented.

- In deciding the level of compensation to be awarded, consideration will be given to the seriousness of the disease being treated, how likely that side effects will occur and any warnings that were given.

- This undertaking to provide compensation extends only to injury arising during the course of the study, but not to injury caused by treatment extended beyond the end of the study commenced by the Investigator.

20 Will my taking part in this study be kept confidential?

Cancer Research UK is the sponsor for this trial based in the United Kingdom and will act as data controller for this study.

Cancer Research UK use personally-identifiable information to conduct research to improve health and care. As a charity, they have a legitimate interest in using information relating to your health and care for research, when you agree to take part in a clinical trial. This means that they will use your data, collected in the course of a clinical trial, in the ways needed to conduct and analyse the clinical trial.

If you agree to take part in this trial, the study doctors will collect information about you and your cancer during your time on the trial and up until the trial closes (you will not need to make a special visit for this follow-up information to be collected – see Section 6). This information, as well as related health records, will remain strictly confidential at all times. However, these will need to be looked at by people authorised by Cancer Research UK and Bicycle Therapeutics Ltd, the company who make BT1718. People from Regulatory Authorities may also need to look at this information. This is so they can all check that the trial is being carried out correctly.

If any information about you leaves the hospital, we will remove your name, address, hospital number and any other personal information so you cannot be identified. You will only be identified by your initials, date of birth and a study number. Your date of birth will be collect as this is required if we need to report any side-effects you may experience to the Research Ethics Committee (who approved this study) and the Medicines and Healthcare products Agency (MHRA) who oversee all clinical trials in the UK; we also need your date of birth because some blood tests have different ranges depending on age. By signing the consent form you agree to information about you being used for the current trial and for any further research carried out which is linked to this trial or where some information may be useful for an unrelated trial, even if you decide to withdraw from (leave) the current trial. The information used will remain confidential.

By consenting to this trial, you give us permission to review and keep any information on what happens to you as part of this trial, and any research samples taken will be analysed as part of the trial and any leftover samples will be considered a 'gift' and will either be destroyed or used for other research not directly linked to this trial (see Section 22). This information will be written up in the form of a report at the end of the trial and submitted to the MHRA. This data will be kept indefinitely.

The information collected and held by Cancer Research UK will be looked at closely. Cancer Research UK will take all necessary steps to protect the confidentiality of your data. At any time in the future, authorised people within Cancer Research UK, Bicycle Therapeutics, as well as

regulatory authorities or research organisations within the UK and other countries may look at the information. Your information could be used for research in any aspect of health or care and could be combined with information about you from other sources held by researchers, the NHS or government. Other companies who wish to develop BT1718, or who intend to, or have, obtained legal ownership of BT1718 may also look at the information.

You can find out more about how we use your information by contacting your research doctor or research nurse. Cancer Research UK has a data protection officer who can be contacted on dataprotection@cancer.org.uk, who can provide further information about how the Charity will use your data. We recommend you contact your research nurse or doctor first as they will be most familiar with the clinical trial and use of the data. If you are unsatisfied with the information you receive or have any concerns, you can also contact the Information Commissioner's Office (ICO) who will be able to advise you further, https://ico.org.uk.

Your anonymised data may be transferred to locations outside of the UK where the level of protection of privacy of personal data is not the same as in the European Economic Area (EEA). However, Cancer Research UK has committed itself to process the personal data of the residents of the EEA in accordance with the rules that apply within the EEA, to protect your privacy and ensure compliance with the UK Data Protection Act of 2018.

The information collected will be kept by your NHS hospital and Cancer Research UK for at least 25 years after the clinical trial has closed.

21 Involvement of your General Practitioner/Family doctor (GP)

We will tell your GP, and other doctors who may be treating you, that you are taking part in this trial and provide regular updates.

22 What will happen to any samples you give?

Your data and any samples (including biopsies and research blood samples) left after analysis for this trial has been completed may be used in the future for ethically approved medical or pharmaceutical research.

Research blood and biopsy samples will be analysed in order to measure the levels of BT1718 and to assess if there have been any changes since receiving BT1718. Analyses will occur at authorised external laboratories which may be within the UK, the European Union (EU) or outside the EU). In the UK all samples will be managed and stored in compliance with the requirements to the Human Tissue Act (HTA). All data and samples will be identified by your initials and trial number so that they can be linked with each other but will remain confidential (only your doctor or their team within the hospital will be able to identify that they are from you). Any unused samples at the end of the trial will be stored initially at the analysing lab but may be transferred to a longer-term storage facility in the future and may be used for ethically approved medical or pharmaceutical research. These samples will be considered as a 'gift'. If the remaining samples cannot be used, these will be destroyed once all the results are analysed and approved.

Routine blood samples will be analysed at the hospital laboratories and then destroyed as the hospital policy.

23 Will any genetic tests be done?

Yes, details of this can be found in Section 6 (Part D) of this information sheet.

24 What will happen to the results of this clinical trial?

The results of the clinical trial will be available after it ends. A report is sent to the MHRA and the results are usually published in a medical journal. You will not be identified in any report or publication. Should you wish to see the results, or the publication, please ask your study doctor.

A summary of the results is also written up in a report and the main findings are uploaded to the Cancer Research UK website (please see Section 13 for details).

You will not have the right to share in any profits that may arise from research in this clinical trial.

25 Who is organising and funding this clinical trial?

This trial is being organised and funded by Cancer Research UK. The study doctors and hospital may receive a grant which helps to support the study. The hospital may be paid to cover the costs of the study tests. Any reasonable expenses you may incur will be reimbursed to you through the hospital.

26 Who has reviewed the study?

All research in the National Health Service (NHS) is looked at by an independent group of people called a Research Ethics Committee, to protect your safety, rights, wellbeing and dignity. The London Chelsea Research Ethics Committee has reviewed this study and they gave favourable ethical approval. This means they agreed this study meets ethical standards and the study could go ahead.

The Medicines and Healthcare products Regulatory Agency (MHRA) have approved the use of BT1718 for this trial.

This patient information sheet has also been reviewed by an independent Patient and Public Involvement panel to ensure an adequate level of information is provided to you.

27 Further Information and Contact Details

If you require any further information or have any concerns while taking part in the trial please contact one of the following people:

Chief/Principal Investigator:	<insert name>
Telephone number:	<insert contact number>
Research Nurse Telephone Number:	<insert contact number>
Out of hours:	<insert name/role, number e.g. Switchboard number or DECT phone number>
Oncology 24hr helpline	(if applicable) Tel:

Or contact the Cancer Research UK Information Nurses (9.00 a.m. to 5.00 p.m., Monday to Friday):

Freephone number 0808 800 4040

Or Visit:

http://www.cancerhelp.org.uk

If you take part in this trial you will be given a copy of this information sheet and a copy of the signed consent form to keep.

Thank you for taking time to read this Information Sheet

Table 2-Summary of the number of blood samples and the approximate amount of blood to be taken during this part of the clinical trial:

		Research blood samples (before treatment with BT1718)		**Research blood samples (during and after treatment with BT1718)**		**Routine blood samples**		
Visit		Number of times blood collected at each visit	Approx. Amount of blood to be taken at each visit (mL)	Number of times blood collected at each visit	Approx. Amount of blood to be taken at each visit (mL)	Number of times blood collected at each visit	Approx. Amount of blood to be taken at each visit (mL)	Approx. total amount of blood (before and after treatment with BT1718) (mL)
Approx. 7 days before treatment with BT1718		1	4			1	10	**14**
Cycle 1	**Days 1-2**	80 mL				1	10	**90**
	Day 8	2	14			1	10	**24**
	Day 15	2	14			1	10	**24**
Cycle 2	**Day 1**	2	10	2	8	1	10	**28**
Cycle 1 or 2	**Day 8 or 15**	One sample to be taken before or after biopsy procedure. If you are having more than one biopsy with more than one hour between the biopsies then a sample will be taken to go with each biopsy.						**4** (**8** if two biopsies more than 1 hour apart)
Cycle 3	**Day 1**	4	24			1	10	**34**
Other Cycles (e.g. Cycle 4, 6)	**Day 1**	1	4	2	8	1	10	**22**
Off study		3	20			1	10	**30**

Blood volume (approximately):

5 mL = 1 teaspoon
10 mL = 2 teaspoons
15 mL = 1 tablespoon
50 mL = 10 teaspoons or just over 3 tablespoons
100 mL = 20 teaspoons or just over 6 tablespoons

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Patient Initials | | | | Patient Screening Number: **SCR** | | / | | | |

For patients who go on to the main trial: Patient Trial Number: | | / | | |

* Only to be completed on Hospital Copy, where appropriate

CONSENT FORM

– consent for taking part in a clinical study

A Cancer Research UK Phase I Trial: A Cancer Research UK Phase I/IIa clinical trial of BT1718, (A Bicycle drug conjugate) given intravenously in patients with advanced solid tumours.

Short Title: A Phase I/IIa trial of BT1718 in patients with advanced solid tumours.

In order to participate in this clinical study, you must write your initials in each box. If you feel you are unable to initial all of the boxes, please discuss this with your doctor.

Please initial every box

- I confirm that I have read and I understand the information sheet dated **<insert issue date>** (version **<insert version number>.** I have had the opportunity to consider the information, ask questions and I have had these answered satisfactorily. ☐
- I understand that I do not have to take part in this study if I do not want to and that I am free to leave the study at any time. This will not affect the quality of my medical care or my legal rights. ☐
- I understand that authorised individuals from Cancer Research UK, Bicycle Therapeutics Ltd or from Regulatory Authorities or other companies/agencies who wish to develop BT1718 may look at my medical records. This is to check the study is being carried out correctly. I give permission for them to look at my medical records for this study and for any further research carried out which is linked to this study, so long as strict confidentiality is maintained. ☐
- I agree that information about me can be collected, analysed, reported, and shared with others within and outside Europe, as part of healthcare and/or medical research. I understand that my name will not be used and I will not be identified other than by my initials, date of birth (if required) and by my trial number. ☐
- I understand that research samples collected (blood/tissue) may be analysed within the UK, the European Union or this may be outside the Europe Union. ☐
- I agree to give blood and research samples (including blood/tissue for genotyping), as described in this information sheet, for use in this trial clinical trial and for future research. ☐
- I understand that research samples collected (blood/tissue) for genotyping, as described in this information sheet, will undergo genetic (DNA) analysis. ☐

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Short Title: A Phase I/IIa trial of BT1718 in patients with advanced solid tumours.

In order to participate in this clinical study, you must write your initials in each box. If you feel you are unable to initial all of the boxes, please discuss this with your doctor.

Please initial every box

- I understand that blood and tissue samples I give **during** the trial may be kept for future ethically approved research and are considered a 'gift'. ☐

- I understand that if I choose to leave this trial, the information collected about me and my cancer can still be used and that follow-up information may still need to be collected. ☐

- I understand that my GP, or any other doctor treating me, will be told I am taking part in this trial. ☐

- **For female patients of child bearing potential only:**

  I understand that should I become pregnant while receiving BT1718 or within six months of me receiving my last dose of BT1718 I will be asked to give consent for Cancer Research UK to collect confidential information about my health and that of my baby from the study doctor. ☐

- **For male patients only:**

  I am aware that there is a risk of irreversible infertility by participating in this trial. ☐

- **For male patients only:**

  I am aware that should my partner become pregnant while I am receiving BT1718 or within six months of my last dose of BT1718 I will make my study doctor aware of this. ☐

Consent for Research Biopsies

For patients where tumour biopsies are mandatory:

- I agree to undergo the tumour biopsy samples as described in this information sheet for this trial. I understand that if I do not agree to have biopsies taken, I will not be able to take part in the trial. ☐

To be printed on Hospital Notepaper

CONSENT FORM

– consent for taking part in a clinical study

A Cancer Research UK Phase I Trial: A Cancer Research UK Phase I/IIa clinical trial of BT1718, (A Bicycle drug conjugate) given intravenously in patients with advanced solid tumours.

Short Title: A Phase I/IIa trial of BT1718 in patients with advanced solid tumours.

In order to participate in this clinical study, you must write your initials in each box. If you feel you are unable to initial all of the boxes, please discuss this with your doctor.

Please initial every box

For patients where tumour biopsies are optional:

- I agree to undergo the tumour biopsy samples as described in this information sheet for this trial. ☐

- **I agree to take part in the BT1718 clinical trial.** ☐

The question below is for consent to the **OPTIONAL** collection of non-tumour biopsy samples. You can choose **not** to consent to these and still participate in the study. If you do not wish to consent to the biopsy, please leave the box below blank, otherwise please initial the box.

- I agree to undergo the non-tumour biopsy samples as described in this information sheet for this trial. ☐

The question below is for consent to the **OPTIONAL** collection of skin punch biopsy sample. You can choose **not** to consent to these and still participate in the study. If you do not wish to consent to the biopsy, please leave the box below blank, otherwise please initial the box.

- I agree to undergo a skin punch biopsy as described in this information sheet for this trial ☐

To be printed on Hospital Notepaper

CONSENT FORM

– consent for taking part in a clinical study

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Short Title: A Phase I/IIa trial of BT1718 in patients with advanced solid tumours.

In order to participate in this clinical study, you must write your initials in each box. If you feel you are unable to initial all of the boxes, please discuss this with your doctor.

Please initial every box

Signatures:

Name of patient	Signature	Date (Please date your own signature)

Name of Investigator/Doctor taking consent	Signature	Date

Name of witness to consent if required.	Signature	Date

Important information for those Investigators/sub-investigators taking consent:

Please ensure that if you are taking informed consent you have completed the study specific delegation log.

Once the Consent Form has been completed: file original in the Investigator Trial File, one in the patient's medical records and give a copy to the patient.