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PATIENT INFORMATION SHEET

ANIMATE

A phase II study of nivolumab monotherapy in patients with relapsed/refractory Hodgkin lymphoma fit for autologous stem cell transplant who fail to reach complete metabolic remission after first or second line salvage therapy

IRAS No.: 216147

We are inviting you to take part in a research study called ANIMATE

We would like to invite you to take part in a study.

Before you decide whether or not to take part, we will go through this Patient Information Sheet with you and answer any questions you may have, so that you understand why we are running the study and what it would involve for you.

Please take the time to read the information carefully and talk to others about the study if you wish.

Ask us if there is anything you don't understand or if you would like more information. Take your time to decide whether or not you wish to take part.

You are free to decide if you want to take part in this study. If you choose not to take part, this will not affect the care you receive in any way.

You can decide to stop taking part in the study at any time without giving a reason.

If you decide to take part, we will ask you to sign a form to give your consent to take part in the study.

The first part of the Patient Information Sheet provides you with a summary. If you would like to find out more, the sheet goes on to tell you about the purpose of the study and what will happen if you take part.

A glossary is also provided at the end of the Patient Information Sheet to describe any acronyms or abbreviations used.

Important things that you need to know

Summary of the research study

This study is for people who have Hodgkin lymphoma which has either come back (relapsed) after initial chemotherapy, or where initial chemotherapy has not worked well enough ('refractory').

Usual treatment in this situation is 2-4 cycles of chemotherapy ('salvage treatment') followed by an autologous stem cell transplant (a procedure where the patient's own stem cells are collected then given back after receiving intensive chemotherapy).

Previous research suggests that the cure rate after a transplant is high if there has been a very good response to the salvage treatment given first. The best way to monitor response is using a PET-CT scan. A tiny amount of radioactive glucose (sugar) is injected before the scan, which highlights areas where there is still active lymphoma despite treatment. If the PET-CT scan is 'negative' (meaning that the salvage treatment seems to have worked well), patients will usually have stem cells collected and have an autologous stem cell transplant. If the PET-CT scan remains positive however, indicating the salvage treatment has not been effective enough

then further salvage treatment may be offered until such time that the PET-CT scan becomes negative before performing a transplant, to maximise the chances that the transplant will work.

Currently we do not know what the best salvage treatment is. Recently, new drugs have been shown to be safe and effective in patients with Hodgkin lymphoma who have had to have different treatments on several occasions. This study aims to assess how well one of these drugs (nivolumab) works as salvage treatment.

Nivolumab is currently approved for use in Hodgkin lymphoma patients if they have relapsed after receiving stem cell transplantation. We will be testing whether nivolumab is effective if used earlier, before stem cell transplantation.

You are being asked if you would like to participate in this trial because you are currently being offered salvage treatment for your lymphoma. If you decide to take part, after 2 cycles of salvage treatment (or 3/4 cycles if you are receiving treatment with brentuximab vedotin), you will have a PET-CT scan. If that scan is positive (indicating that the salvage treatment has been less effective than we would like), you will be offered trial treatment. This will consist of between 4 and 8 cycles of nivolumab. Each nivolumab cycle lasts 2 weeks, so the extra treatment will take between 2 and 4 months. The length of treatment depends on how effective the treatment is and if you experience treatment side-effects.

We will take regular blood tests and use PET-CT scans to check how the treatment is working.

We will monitor your progress for at least 3 years after the end of your treatment.

Is the treatment safe?

Nivolumab is already used to treat Hodgkin Lymphoma as well as several different cancers, so we know quite a lot about possible side effects. Treatment is generally well tolerated, and the side effects are usually manageable. The most common side effects include diarrhoea, a skin rash and feeling tired or weak.

Uncommon side effects can happen because nivolumab works by affecting the immune system and can cause inflammation in parts of the body. Although uncommon, inflammation may cause serious damage to your body requiring hospital admission and occasionally treatment for life threatening conditions.

During the study, we will closely monitor how you are doing.

Although unlikely, it is possible that new side effects could be identified during the study that we don't already know about.

Will I have any extra visits or tests?

- Nivolumab treatment is given every 2 weeks. This may be more frequent than some other salvage treatments.
- In addition to routine blood tests, we will ask you to have up to ~~12~~ 6 extra blood samples taken during the course of the study. These can be taken at the same time as your usual blood tests and no extra visits will be required.
- If you are a woman who could become pregnant, you will have regular pregnancy tests before, during and after trial treatment.
- You will be asked to have up to 3 breathing (lung function) tests during the trial. These would not be done if you were not taking part in the trial, but are needed to check for lung damage due to nivolumab, which may need treatment.

- If you are still PET positive after 8 cycles of nivolumab, you will be asked to have an additional lymph node biopsy, but this is optional.

If you have questions

We hope you find this information sheet helpful. We appreciate it may not answer all of your questions, so please do not hesitate to contact us on the telephone numbers given at the end of this Patient Information Sheet if you would like to discuss any aspect of the study further.

Thank you

Thank you for reading his information.

If you take part, you will help us to understand more about this disease and its treatment.

This may help future people with Hodgkin lymphoma.

Contents

1. Why are we doing this study?

This study is for patients with Hodgkin lymphoma which has either come back after (relapsed) initial successful treatment, or has not responded well enough to initial treatment.

Currently, standard treatment is a combination of chemotherapy drugs (called 'first line' salvage treatment), followed by an assessment with a PET-CT scan. If the PET-CT scan has become negative (meaning that the disease has been effectively treated), patients are usually offered a transplant using their own stem cells straight away or after a further cycle of the same chemotherapy.

Having a negative PET-CT scan before having a stem cell transplant is important because previous research has shown that the chance of cure after transplant is much greater if the PET-CT scan beforehand is negative. Therefore, if patients have a positive PET-CT scan after first line salvage treatment, they often go on to have more ('second line') salvage treatment to try and achieve a negative PET-CT scan.

Currently, we do not know what the best salvage treatment is in this situation. Patients are usually offered either a different combination of chemotherapy drugs, or the drug brentuximab vedotin. Although brentuximab vedotin is being used more often, only about 1 in 3 patients achieve a negative PET-CT scan after brentuximab vedotin, and often responses do not last long.

Nivolumab is a new medicine which works in a different way to usual chemotherapy and brentuximab vedotin. It is an antibody which activates cells in the immune system, so they can attack the cancerous cells of Hodgkin lymphoma. Previous studies in patients with difficult-to-treat Hodgkin lymphoma have shown it to be safe and effective. Currently it is approved for treatment in Hodgkin lymphoma, but only in patients who have relapsed after receiving stem cell transplantation. It has

not yet been studied as a salvage treatment before receiving stem cell transplantation.

2. Why have I been invited to take part?

You have been invited to take part in this study because you have classical Hodgkin lymphoma which has either returned following initial successful therapy, or has not responded well enough to initial therapy ('refractory' disease), and you are receiving first or second line salvage treatment. Your doctor feels that you are fit enough to be considered for stem cell transplant.

Patients will be enrolled in the trial before having a PET-CT scan which will decide whether they have the trial treatment (nivolumab) or not. Only patients with a positive PET-CT scan will be eligible to ~~take~~ have the new drug.

If your PET scan is negative, we will still gather very useful information from your participation in the trial even though you won't be treated with the trial drug. For example, ~~we plan to do~~ tests will be done on your previous biopsies to see if we can learn about biological features which help to predict a good response to chemotherapy.

We are aiming to treat 30 patients with nivolumab. As most patients will have a negative PET-CT scan after first or second line salvage treatment, we estimate that we will need 75-120 patients to enrol in the study during salvage treatment to identify 30 patients who are suitable for treatment with nivolumab.

3. What will happen to me if I take part?

During your first or second line salvage treatment, your doctor will discuss the trial with you and give you the chance to decide whether or not to take part. We will give you plenty of time to read this information, discuss it with anyone you wish, and ask questions. If you agree to take part, you will be asked to sign a consent form. You will be given a copy of the signed form to keep.

You will then enter the 'screening' period of the study. Your doctor will ask about your medical history and consult your medical notes. If you are a woman who could potentially become pregnant, you will have a pregnancy test. If these investigations show that you are eligible for the trial, you will be registered as a trial patient. Tissue from a previous biopsy of your lymphoma, which is currently stored in your hospital's pathology department, will be sent to the Haematological Malignancy Diagnostic Service in Leeds and analysed in further detail so we can learn more about the biology of lymphoma and how to predict who will respond well to salvage treatment.

Screening will happen whilst you are receiving your salvage therapy. After 2 cycles of salvage treatment (or 3/4 cycles of brentuximab vedotin), you will have a PET-CT scan. Although you would have this scan regardless of whether you take part in the trial or not, the scan will be performed in a certain way to enable us to use the scan as part of the trial. Because not all hospitals have PET scanners that can perform trial scans, you may need to go to a different hospital to have your PET-CT scan – your study doctor will tell you which hospital would be doing your trial scans.

You will need to have a CT scan with intravenous contrast given through a cannula into a vein. This contrast injection will give a more detailed picture of the lymphoma. At some hospitals, this can be done at the same time as the PET scan, but at others it may require a second scan. The CT scan with contrast may not be needed in patients who are not part of the study.

The PET-CT scan and contrast enhanced CT scan images will be pseudonymised ~~anonymised~~ (only your initials and trial

number will be included on the images) and sent securely to St Thomas' Hospital London, where they be reviewed by experts. The experts will also be sent images from the scan you had performed before salvage, and will compare the two scans to see how well your lymphoma has responded.

If your PET-CT scan is negative then you will not receive the study drug (nivolumab). You will continue with standard treatment for your lymphoma, which may mean you are offered a stem cell transplant either straight away, or after one more cycle of salvage chemotherapy. After the stem cell transplant, you will be seen in clinic regularly, and data will be collected for the trial, to allow us to see how you are doing, every 3 months for 1 year and then every year for a minimum of 3 years.

If the PET-CT scan is positive, we will perform additional tests to check that you are well enough to receive nivolumab. These will include blood tests, a heart tracing (called an ECG) and a repeat pregnancy test (if applicable). Most of these will be done as part of your usual care, but extra blood tests will be done and you will be asked to perform additional breathing (or lung function) tests. This is to make sure that you do not have any immune conditions that might cause you problems whilst receiving nivolumab.

If these tests are alright, you will receive up to 8 cycles of nivolumab. Treatment is given once every two weeks (2 weeks = 1 cycle of treatment). Nivolumab is given into a vein, either through a cannula inserted into the back of the hand or the arm, or through a line. The infusion takes approximately 1 hour to give, and usually there are no other medications given before the infusion.

Before each infusion of nivolumab is given, you will be assessed by a member of the medical and nursing team. They will ask you about any new symptoms you may have experienced and whether you are taking any new medications. They will perform a physical examination, and you will have a blood test performed to check it is safe to proceed with treatment.

You will have additional blood taken for research purposes. Just under 4 tablespoons of blood (55ml) will be taken before starting nivolumab, then a smaller amount (25ml) will be taken before starting cycles 2, 4, 6 and 8 and 1 month after stopping nivolumab. These blood samples will be sent to two laboratories: the Weatherall Institute of Molecular Medicine, Oxford, and then the MRC – University of Glasgow Centre for Virus Research, where they will be analysed in order to help us understand how the drug is working in Hodgkin lymphoma, and whether we can use 'biomarkers' from blood tests to monitor response to the drug.

After 4 cycles of nivolumab (approximately 8 weeks) you will have another PET-CT scan using the same method, and the same scanner, as your pre-treatment PET-CT scan. You will also have a contrast enhanced CT scan. As before, the scan images will be pseudonymised (marked with your study number instead of your name) ~~anonymised~~ and sent securely to experts at St Thomas' Hospital, London and compared to your previous scans:

- If the PET-CT scan is negative, then no further nivolumab will be given, and your doctor will discuss what further treatment you will have. For example, you may be offered a stem cell transplant.
- If the PET-CT scan suggests growth of the tumour ('disease progression') you will not receive more nivolumab and your doctor will discuss alternative treatment options with you.
- If the PET-CT scan is positive but there is no evidence of disease progression,

you will have 4 more cycles of nivolumab, taking approximately another 8 weeks.

After cycle 8 of nivolumab, you will have a PET-CT scan performed in the same way, and on the same scanner, as before. You will also have a contrast enhanced CT scan. Again, the scan images will be pseudonymised ~~anonymised~~ and sent securely to experts at St Thomas' Hospital, London and compared to your previous scans:

- If the PET-CT scan is negative, you will probably be offered a stem cell transplant.
- If the PET-CT scan is positive, your doctor will discuss with you any alternative treatments available.
  With your permission, ~~we would also like you to have~~ a biopsy of the PET positive area will be taken. This is to check that the positive PET scan indicates persistent lymphoma. Because nivolumab activates the immune system, it may result in increased activity of normal cells in lymph nodes (or glands) on PET scan, which may be mistaken for lymphoma even after the lymphoma has been eradicated. The biopsy will help us to understand whether PET-CT is a good way of assessing response to nivolumab.

After completing trial treatment, you will be seen in clinic for the trial every month for 3 months, then every 3 months until 1 year after the end of your treatment. At these visits you will have blood tests. After this, we will collect information on your disease status every year for at least 2 years.

Patients who have study treatment will have breathing (lung function) tests carried out before nivolumab treatment, at the end of treatment and one year after treatment. This is because nivolumab can damage the lungs and we need to check that the drug is safe, and that any damage gets better. If any lung damage is identified, you will receive appropriate treatment. You would not have lung function tests if you were not taking part in the trial.

Please see appendix 3 for a diagram summarising the ANIMATE treatment pathway. Appendix 4 gives a full list of tests you would have if you decided to take part in the trial.

4. What will I have to do?

You will be required to attend hospital for up to 3 PET-CT scans. At some hospitals the PET-CT scans and contrast CT scans can be done on the same scanner, at others you may have to have 2 scans but these would ideally be arranged on the same day to minimise the number of visits.

Patients who are eligible to receive nivolumab will be required to attend for treatment (up to 8 visits, every 2 weeks) and lung function tests (up to 3 tests).

You should tell your study doctor or nurse about any drugs you are taking at the moment, and any changes in your health, lifestyle or the medication you are taking during your trial treatment.

You should also tell your study doctor or research nurse if you experience any side effects during nivolumab or up to 4 months after completing treatment.

All patients will need to attend for follow up visits. In patients who do not receive trial treatment, these will be:

- Every 3 months for 1 year
- Annually thereafter for at least 2 years

In patients who receive trial treatment, follow up visits will be:

- Every month for 3 months
- 3-monthly until one year post treatment

- Annually thereafter for at least 2 years

If your care is moved to another hospital that is not taking part in the ANIMATE trial during the follow up period, your study doctor will be sent copies of your clinic letters or may contact your GP to find out how you are, and to find out about any more lymphoma treatment you have had. They will continue to send information on your disease status to UCL CTC unless you have told them that you do not wish to carry on with the trial (see section 12 of this leaflet for more information about what happens if you don't want to carry on).

5. What are the side effects of any treatment received when taking part?

Nivolumab is a relatively new drug. It is licensed in Europe for use in certain types of skin cancer, lung cancer and Hodgkin lymphoma that has relapsed after a stem cell transplant. In clinical trials, nivolumab has consistently shown fewer side effects than standard chemotherapy. However, as this study is testing nivolumab in a new group of patients, we may see some side effects more or less often, and they may be more or less severe than in other patient groups. There is also a chance that there may be other side effects that have not been seen in other groups of patients.

Nivolumab is an antibody which activates the cells of the immune system to attack and kill cancer cells. Sometimes, however, the activated immune system cells can attack the normal cells of the body, causing so-called 'immune-related adverse effects'. Examples include pneumonitis (inflammation of the lungs) and colitis (inflammation of the large bowel or colon). These can range from mild to severe and on occasion life-threatening. ~~In addition, CMV infection or reactivation has been associated with Nivolumab treatment with reported cases of CMV induced hepatitis and colitis. Symptoms of colitis would be~~Please get in touch with your study doctor if you experience abdominal pain, cramping, diarrhoea or blood in the stool.

Other immune-related ~~S~~symptoms include:

- Itching
- Rash
- ~~Diarrhoea~~
- ~~Stomach pain~~
- Tiredness
- Weight gain
- Weight loss
- Palpitations
- Symptoms of jaundice (yellowing of the eyes or abdominal pain)
- Shortness of breath

If you develop an immune-related adverse effect, you will receive treatment for the symptoms. Your trial treatment may be stopped temporarily or permanently, and you may receive steroid treatment.

Sometimes you will not have any symptoms but blood tests and lung function tests will show you have inflammation; if this is the case your doctor will discuss this with you further and may offer you treatment for the inflammation.

Studies have shown that nivolumab can rarely~~sometimes~~ cause a virus called cytomegalovirus (CMV) to become active again; many people have CMV infection as children and the virus stays dormant in the body afterwards. If you have symptoms like those listed above (i.e. abdominal pain, cramping, diarrhoea or blood in the stool) that do not get better with steroids, your doctor may do blood tests to see if you have CMV infection that needs treatment with antiviral drugs.

Other common side effects seen in patients given in nivolumab include:

- Fatigue (tiredness)
- Nausea (feeling sick)

- Decreased appetite
- Weakness or lack of energy.

Some patients treated with nivolumab experience an allergic reaction to the infusion. In rare cases (less than 1% of patients) these can be severe ('anaphylactic reaction'). You will be monitored closely during your infusions. If you do have an infusion reaction, the treatment will be stopped. Depending on how severe the reaction is, you may not receive nivolumab again, or you may need to be given drugs alongside nivolumab to prevent allergic reactions.

The company that make nivolumab have warned that some patients may feel tired (fatigued) during treatment, which may affect their ability to drive or operate machinery safely. You are advised to avoid driving or operating machinery after attending for your first dose of nivolumab, or if you are experiencing fatigue during or after treatment.

Complications, including fatal events, have occurred in patients who had an allogeneic stem cell transplant (a transplant where they received another person's stem cells) before or after nivolumab. Complications, including rejection, have also been reported in patients who have received an organ or tissue transplant. Treatment with nivolumab may increase the risk of rejection of the transplanted organ or tissue.

The company that make nivolumab have warned that a very small number of people (≥1/10,000 to < 1/1,000) taking nivolumab for Hodgkin lymphoma and other cancers have developed severe skin reactions known as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis. These illnesses are not specific to nivolumab; a number of other drugs are known to cause them. However, although they are usually treatable it can be severe and may be fatal. The main symptoms are a rash and blistering of the skin. If you develop a rash during or after your nivolumab treatment, please contact your study doctor immediately.

You may experience some, or none, of the symptoms listed above. For a full list of possible side effects please see appendix 2 at the end of this leaflet.

When you come for your hospital visit, we will ask you about any side-effects you have experienced. It is important that you tell us about any problems, as it is often possible to deal with side effects by adjusting the study treatment (for example by giving you a treatment break to recover) or giving you some other medication. We will monitor you closely for any possible side effects and we may suggest additional investigations if we consider it appropriate.

If you become suddenly unwell between hospital visits and especially if you develop the symptoms of immune-related adverse effects listed above, please telephone us immediately for advice, as you may need to be admitted to hospital.

When you join the study, we will give you a contact card to let you know the correct number to call. You should carry this with you at all times. If you are admitted to a hospital or have to see your GP in between hospital visits, please remember to show them the contact card in case they need to speak us.

6. Are there any other risks?

If you take part in this study you will have up to 3 PET-CT scans, some of which will be extra to those that you would have if you did not take part. These procedures use ionising radiation to form images of your body to provide your doctor with information about how treatment is working. Ionising radiation can cause cell

damage that may, after many years or decades, turn cancerous.

The chances of this happening to you as a consequence of taking part in this study are 0.4%. For comparison, the natural lifetime cancer incidence in the general population is about 50%.

7. Pregnancy and Contraception

For female patients:

Please share this information with your partner if appropriate.

It is not known if nivolumab is harmful to unborn babies.

If there is a chance that you could become pregnant, we will ask you to take a pregnancy test (urine or blood) before entering the study to ensure you are not pregnant. We will repeat pregnancy testing before treatment, monthly throughout treatment and for 2 months after completing trial treatment, to confirm you are not pregnant.

If you are currently, or could be, sexually active with a man, you must agree to use at least 2 forms of contraception during your treatment: condoms and a hormonal form of contraception e.g. contraceptive pill, injection, implant, intrauterine device (IUD; 'coil') or intrauterine hormone-releasing system (IUS; 'Mirena coil'). This must continue for the time you are receiving treatment and for at least 6 months after you finish your treatment.

If you do become unexpectedly pregnant during the study, you must inform us immediately. We would discuss referral for specialist counselling on the possible risks to yourself and your unborn baby.

Women who become pregnant whilst on the trial will need to stop treatment immediately.

We would also like to monitor any pregnancies occurring during trial treatment and where conception is within the 6 months following trial treatment, provided you give your consent.

If you consent, we will collect information about the pregnancy, details of any previous pregnancies and information about medications you have been taking. We will want to continue to collect information for up to 8 weeks after the end of the pregnancy to collect information on ante- and post-natal problems, whether the pregnancy continued to term and if so, how the baby was after birth. This information is important because it helps us to better understand the effect of the trial treatment on pregnancy and the unborn baby.

Information relating to your pregnancy will also be shared with Bristol-Myers Squibb, who are providing nivolumab for use in the trial, so they can monitor the safety of their drug, however it will not be possible to identify you from the information they are provided.

Whether or not you allow us to collect information about your pregnancy is entirely voluntary. If you do agree, we will ask you to initial the pregnancy monitoring section in the main consent form to show that you have agreed to allow us to collect the information. If you decide that you do not want to allow us to collect this information, or if you agree and then later change your mind, this will not affect the care you receive in any way. If you change your mind we will stop collecting any more information, but information that has already been sent to the organisers of the study will be kept by them.

For male patients:

Please share this information with your partner if appropriate.

It is possible that nivolumab will affect sperm or semen and therefore you should not father a child during study treatment or for 8 months after you finish your treatment.

If there is a possibility that your partner might become pregnant, you must use at least 2 form(s) of contraception during your treatment and for 8 months afterwards: condoms and a hormonal form of contraception e.g. contraceptive pill, injection, implant, intrauterine device (IUD; 'coil') or intrauterine hormone-releasing system (IUS; 'Mirena coil'). If your partner becomes pregnant during your study treatment, or within 8 months of your stopping treatment, you must tell us immediately. We would discuss referral for specialist counselling on the possible risks to your partner and your unborn baby.

We would also like to monitor any pregnancies by your partner that occur during or following your study treatment provided your partner gives their consent. We will give your partner a pregnancy monitoring information sheet and consent form if they become pregnant and we will ask them to give their consent for us to monitor their pregnancy.

If they consent, we will collect information about the pregnancy, details of any previous pregnancies and information about medications they have been taking. We will want to continue to collect information for up to 8 weeks after the end of the pregnancy to collect information on ante- and post-natal problems, whether the pregnancy continued to term and if so, how the baby was after birth. This information is important because it helps us to better understand the effect of the trial treatment on pregnancy and the unborn baby.

Whether or not they will allow us to collect information about their pregnancy is entirely voluntary. If they do agree, we will ask them to sign a pregnancy consent form to show that they have agreed to allow us to collect the information. If they decide that you do not want to allow us to collect this information, or if they agree and then later change their mind, this will not affect the care you receive in any way. If they change their mind we will stop collecting any more information, but information that has already been sent to the organisers of the study will be kept by them.

8. What are the possible advantages and disadvantages of taking part?

Advantages

We cannot promise the study will help you, but we hope the information we receive from you taking part in this study will help improve our knowledge of treating Hodgkin lymphoma which will benefit the treatment of people with Hodgkin lymphoma in the future.

Disadvantages

The disadvantages of taking part in the study are mostly associated with the side effects of the study treatment mentioned in Section 5. If you decide to take part in this study you will need to attend the hospital more than if you were to receive treatment outside of the study. This involves extra travel and inconvenience. You may also need to have extra tests at each of these visits, and may have to have additional PET-CT scans. Unfortunately, travel costs cannot be reimbursed by the study sponsor, but individual trial sites may be able to cover these – please ask your study doctor or research nurse about this.

Before participating in this study, you should consider if taking part will affect any insurance you have and seek advice if necessary.

9. What happens when the study stops?

When the study stops, your doctor will offer you alternative treatment for your lymphoma if and when you need it.

10. What are the alternatives for treatment?

Standard salvage treatment for Hodgkin lymphoma varies. It may consist of combination chemotherapy, or a single targeted drug such as brentuximab vedotin, and is often followed by an autologous transplant (a transplant using the patient's own stem cells). At some hospitals, patients are offered a stem cell transplant using cells from a brother, sister or unrelated donor (an 'allogeneic transplant'), especially if the response to salvage is not very good.

The standard salvage treatments can be effective, but combination chemotherapy and allogeneic transplants can cause a lot of side effects. Only about 1 in 3 patients achieve a negative PET scan following brentuximab vedotin, and remissions do not tend to last very long.

11. Do I have to take part?

No. It is up to you to decide whether or not to take part in the study. We will describe what would be involved and go through this Patient Information Sheet with you, which is yours to take away so that you have the opportunity to read it carefully and discuss with others if you wish. If you decide to take part, we will ask you to sign a consent form of which you will be given a copy. You are free to withdraw at any time, without giving a reason. If you decide not to take part, or later to withdraw, this will not affect the care you receive from us in any way.

12. More information about taking part

Who is conducting the study?

University College London (UCL) is the Sponsor and Data Controller for this study and it is run on their behalf by Cancer Research UK & UCL Cancer Trials Centre (UCL CTC), based in the United Kingdom. UCL CTC will be using information from you and your medical records in order to undertake this study. This means that UCL CTC are responsible for looking after your information and using it properly. UCL CTC will keep identifiable information about you for at least 25 years after the study has finished.

Details about you, your treatment, any side effects you have, how the cancer responds and how you are during and following study treatment will be recorded in your medical notes. We will keep identifiable information about you from this study for at least 25 years after the study has finished. The study information collected will be used to help improve our knowledge of Hodgkin lymphoma. This research is conducted in the public interest as it may lead to improvements in future treatment.

Your rights to access, change or move your information are limited, as UCL CTC need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, UCL CTC will keep information about you that they have already obtained. To safeguard your rights, UCL CTC will use the minimum personally identifiable information possible.

You can find out more about how UCL CTC will use your information on UCL CTC's website:
http://www.ctc.ucl.ac.uk/Privacy.aspx

If you wish to raise a complaint on how UCL CTC have handled your personal data, you can contact their Data Protection Officer who will investigate the matter. If you are not satisfied with their response or believe they are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO).

UCL's Data Protection Officer can be contacted on data-protection@ucl.ac.uk

How will my data be handled during the study?

When you join the study you will be assigned a study number by UCL CTC, which will be used instead of your name and will be linked to all of your study data. This is called 'pseudonymised data', and you cannot be directly identified from this.

We will pass your initials, date of birth and NHS/CHI number to UCL CTC along with the information collected from you and your medical records. Your initials, study number and date of birth will also be marked on any blood and tissue samples and PET-CT scan images you agree to being collected and sent to the central laboratory (the Haematological Malignancy Diagnostic Service in Leeds, the Weatherall Institute of Molecular Medicine in Oxford, The MRC-University Glasgow Centre for Virus Research and the UK PET Core Laboratory and St Thomas' Hospital, London). This is to make sure that your samples and scan images are not mixed up with those from other patients. The laboratoryies will make sure your information is held securely and not shared with anyone else.

Your medical records may also be looked at by appropriate individuals from UCL CTC, UCL or its representatives, Bristol-Myers Squibb who are providing drug for the trial, regulatory authorities and your NHS Trust/Health Board. This is to ensure that the study is being carried out properly and that the information collected is accurate.

UCL CTC may also collect information about you to follow your progress once your study treatment and visits have finished from NHS Digital (England), NHS Wales Informatics Service (Wales) or the Information Services Division (Scotland). To do this, UCL CTC will need to provide them with your NHS/CHI number.

Information relating to any serious side effects you may experience, including ~~adverse events of special interests~~any immune-related side effects~~ where necessary~~ and pregnancies will be sent by UCL CTC to Bristol-Myers Squibb, who are providing nivolumab for the study, and are based in the USA, so they can monitor the safety of their drug. All information will be pseudonymised before it is sent to Bristol-Myers Squibb, so they will not be able to directly identify you. Your data will be sent outside the UK for safety reporting purposes, and UCL CTC will take reasonable steps to ensure that the principles of the Data Protection Act are maintained.

These organisations will always keep information about you confidential.

Your name or identifiable data will not be used in any reports about the trial.

~~**How will my data be handled? Who will know that I am taking part in the study**~~

~~Details about you, your treatment, any side-effects you have, how the cancer responds and how you are during and following study treatment will be recorded in your medical notes. The study information collected will be used to help improve our knowledge of treating Hodgkin lymphoma. This research is in the public interest as it may lead to improvements in future treatment.~~

~~Your name will not be used in any reports about the trial.~~

University College London (UCL) is the sponsor for this study based in the United Kingdom. We will be using information from you and your medical records in order to undertake this study, and will act as data controller for this study. This means that we are responsible for looking after your information and using it properly. UCL will keep identifiable information about you for at least 25 years after the study has finished, as is required by law for clinical trials.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep information about you that we have already obtained. To safeguard your rights, we will use the minimum personally identifiable information possible.

You can find out more about how we use your information on UCL CTC's website: www.ctc.ucl.ac.uk/privacy. This includes details of how to contact UCL's data protection officer and how to make complaints to the Information Commissioner's Office (ICO)

This study will be registered under the UK Data Protection Act 2018 through UCL. When you join the study you will be assigned a study number by UCL CTC. This study number will be used instead of your name, and will be linked to all of your study data. This is called 'pseudonymised data', and you cannot be personally identified from this. Your study number will also be used to link your study data to the tissue and blood samples and PET-CT scan images you agree to being collected and sent to relevant central laboratories (the Haematological Malignancy Diagnostic Service in Leeds, the Weatherall Institute of Molecular Medicine in Oxford, The MRC-University Glasgow Centre for Virus Research and the UK PET Core Laboratory and St Thomas' Hospital, London).

Your hospital will collect information from you and your medical records for this research study in accordance with our instructions.

Your hospital will use this information as needed, to contact you about the research study, to make sure that relevant information for the study is recorded for your care, and to oversee the quality of this study.

Your hospital will pass your initials, date of birth and NHS/CHI number to UCL CTC along with the information collected from you and your medical records. Your initials and date of birth will also be marked on samples and scans sent to relevant central laboratories. This is to make sure that your samples and scans are not mixed up with those for other patients. These laboratories will make sure your information is held securely and not shared with anyone else.

Representatives of the sponsor, UCL, regulatory organisations, Bristol Myers Squibb, who are providing drug for the trial, and your NHS Trust/Health Board may look at your medical and research records to check the accuracy of the research study.

The only people at UCL who will have access to information that identifies you (your initials, date of birth and NHS number) will be people directly involved in the trial, or who audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name or contact details.

Your hospital will keep identifiable information about your from this study for at least 25 years after the study has finished.

UCL CTC may also collect information about you from NHS Digital and national health registries to obtain health information,

which is regarded by law as a 'special category' of information, to help us conduct this research study. We will only do this if, for some reason, your study visits come to an end before the end of the trial. Your NHS/CHI number will be used as part of this information request.

Will my GP be informed that I am taking part in this research study?

We will tell your GP about your participation in the study. We may also contact your GP to obtain information about your health status in some cases, for example if you miss a study visit. Your hospital will tell your GP about your participation in this study. Your hospital may also contact your GP to obtain information about your health status in some cases, for example if you miss a study visit.

Who will my study data be shared with?

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies, in UCL and other organisations, such as universities, the NHS or companies involved in health and care research in the UK or abroad. Your data will only be used in research that has been independently reviewed by an ethics committee.

Wherever possible UCL CTC will not share any information that can identify you, or that can be combined with other information in a way that could identify you, however we may share your trial number. The information will only be used for the purpose of health care research and cannot be used to contact you or affect your care. It will not be used to make decisions about future services available to you, such as insurance.

Information regarding any serious side effects you may experience, including immune-related effects, and pregnancies will be shared with Bristol Myers Squibb, who are providing nivolumab for the study, and are based in the USA, so that they can monitor the safety of their drug. We will anonymise this information before it is sent to Bristol Myers Squibb, so they will not be able to identify you. Your data will be sent outside the UK for safety reporting purposes, and UCL CTC will take reasonable steps to ensure that the principles of the Data Protection Act are maintained.

What if relevant new information becomes available?

Sometimes we get new information about treatments being studied. If this happens, your doctorwe will tell you and discuss with you whether you should continue in the study. If you decide not to carry on, your doctorwe will make arrangements for your care to continue outside the study. If you decide to continue in the study, you may be asked to sign an updated consent form.

In some circumstances, your doctorwe might consider it best for you to withdraw from the study. If this is the case, your doctor will explain the reasons and arrange for your care to continue outside the study.

If the study is stopped for any other reason, your doctorwe will tell you and arrange your continuing care.

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

As described earlier, you can withdraw from the study at any time without giving a reason and without your rights being affected but we UCL CTC would like to continue to collect information about you, so that we they know about your progress following study treatment. We They will also need to use the information collected up to your withdrawal. Any stored blood or tissue samples that can be identified as yours will be destroyed if you wish.

What if there is a problem?

Every care will be taken in the course of this clinical trial. However, in the unlikely event that you are injured by taking part, compensation may be available. If you suspect that the injury is the result of the Sponsor's (University College London) or the hospital's negligence, then you may be able to claim compensation. After discussing with your study doctor, please make the claim in writing to Dr Graham Collins, who is the Chief Investigator for the clinical trial, and is based at the Churchill Hospital, Oxford. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. If you have a claim then it might be helpful to consult a lawyer. ~~You may have to bear the costs of the legal action initially, and you should consult a lawyer about this. Participants may also be able to claim compensation for injury caused by participation in this clinical trial without the need to prove negligence on the part of University College London or another party. You should discuss this possibility with your study doctor in the same way as above.~~

Regardless of this, should you wish to complain, or have any concerns about the way you have been approached or treated by members of staff, or about any side effects ~~('adverse events')~~ you may have experienced due to your participation in the clinical trial, the normal National Health Service complaints mechanisms are open to you. Please ask your study doctor if you would like more information on this. Details can be obtained from the NHS website. ~~Details can also be obtained from the Department of Health website: http://www.dh.gov.uk.~~

What will happen to the samples I give?

Routine blood tests will be carried out ~~at your hospital~~ before, during and after treatment to check your blood counts and your blood biochemistry. These will be analysed ~~at your hospital~~by us and any leftover samples will be discarded.

Some extra tests are needed to check it is safe for you to continue with trial treatment – these include blood tests and, where applicable, pregnancy tests. ~~These will be carried out at your local hospital, and w~~Wherever possible these will be carried out ~~on~~ using your routine blood samples. You should not need to have extra visits for these tests to be performed. In addition to your routine blood tests, we would also like to collect some samples for research purposes:

- Blood samples:
  - 55ml (just under 4 tablespoons) from patients who are PET positive after first or second line salvage treatment, before receiving nivolumab;
  - 25ml (just under 2 tablespoons) before cycles 2, 4, 6 and 8, and one month after completing nivolumab.

  These samples will be sent to two laboratories: the Weatherall Institute of Molecular Medicine, Oxford, and then MRC University of Glasgow Centre for Virus Research, where they will be analysed.
- Tumour biopsy samples:
  - Stored tissue from a tumour biopsy (taken either at relapse or when you were first diagnosed with lymphoma) will be sent to the central laboratory for all registered patients (this is a sample that is already stored at your hospital).
  - A repeat biopsy if you have a positive PET-CT scan after 8 cycles of nivolumab. This sample is optional, and you can take part in the study even if you do not wish to have a repeat biopsy. However, we think

these samples could give us useful information about whether PET-CT scanning is a good method of checking response to nivolumab.

- If your lymphoma relapses after receiving nivolumab and a biopsy is taken, we will ask for part of this biopsy to be used for research. A repeat biopsy will only be performed if recommended by your doctor as part of your routine treatment.

These samples will be sent to the Haematological Malignancy Diagnostic Service in Leeds, where they will be analysed.

The central laboratories will carry out tests to look at features of lymphoma and signs of response to treatment.

Samples will be marked with your trial number, initials and date of birth.

With your permission, ~~we~~ UCL CTC would like to keep any leftover material from the samples for use in future research studies which could help us learn more about Hodgkin lymphoma. Like this trial, any studies that used your leftover samples would have been reviewed and approved by a Research Ethics Committee. Donating your leftover samples for future research is optional, and you can take part in this study even if you do not wish to donate leftover samples for future research. If you allow us to store samples, but later change your mind, please let your study doctor know, and ~~we~~ UCL CTC will arrange for your stored samples to be destroyed.

Will any genetic tests be done?

A test called 'gene expression profiling' will be carried out on your tumour biopsy sample. This does not look at your normal genes, but rather at the genes of your cancer cells. If we can understand the genetics of cancer cells better, we may be able to develop more effective treatments in future.

What will happen to the results of the study?

~~We~~ UCL CTC will publish a summary of results on ~~the UCL CTC~~their ~~study~~ website, the European Clinical Trials Register, Cancer Research UK's website and in ~~a~~ medical journals, so that other researchers can see them.

~~We~~ They will also send a separate summary of the study results to ~~your study doctor who~~us so that we can ~~will~~ discuss them with you.

Your identity and any personal details will be kept confidential. No named information about you will be published in any report of the study.

Who is organising and funding the research?

The study is funded by Bristol-Myers Squibb Pharmaceuticals Ltd, sponsored by University College London, and run by Cancer Research UK & UCL Cancer Trials Centre (UCL CTC).

Nivolumab for use in the trial is being provided by Bristol-Myers Squibb Pharmaceuticals Ltd. Bristol-Myers Squibb are also providing funding to cover the cost of managing the trial at UCL CTC, laboratory work, and some of the research costs associated with the trial. UCL CTC also receives additional funding from Cancer Research UK.

Your doctor will not be paid for including you in the study, but the sponsor of the study, where appropriate, will reimburse the hospital sites with some of the research costs involved in running the study.

How have patients been involved in the study?

In designing this study, ~~we~~ UCL CTC have taken into account patient opinions on the information provided in this Patient Information Sheet.

Members of the National Cancer Research Institute's Lymphoma Clinical Studies Group have been involved in reviewing the content of the Patient Information Sheet and have provided helpful comments.

There is also a patient representative on the Trial Management Group which oversees the running of the trial.

Who has reviewed the study?

All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect the interests of any patients that may take part. This study has been reviewed and granted a favourable opinion by the London – South East Research Ethics Committee and has also been approved by the Research and Development department at your hospital.

The study has also been peer reviewed by independent lymphoma experts from across the world, the National Cancer Research Institute's Lymphoma Clinical Trials Group and an independent statistician.

Thank You

Thank you for considering taking part in this study and for taking the time to read this Patient Information Sheet, which is yours to keep. If you decide to take part in the study, you will also be given a copy of your signed consent form.

Further Information

You may wish to contact one of the following organisations that are independent of the hospital at which you are being treated:

- **Macmillan Cancer Support** provides practical, medical and financial support and work towards the improving cancer care. They can be contacted at:

  Tel: 0808 808 00 00 (Freephone)

  Or visit their website at:

  http://www.macmillan.org.uk/HowWeCanHelp/HowWeCanHelp.aspx

- **CancerHelp** (Cancer Research UK), who provide all aspects of information for people with cancer. Their contact details are:

  Tel: 0808 800 4040 (Freephone)

  Or visit their website at:
  http://cancerhelp.cancerresearchuk.org

- **Lymphoma Action** – a charity organisation providing information and support to people affected by all types of lymphoma. Their contact details are:

  Tel: 0808 808 5555 (Freephone)

  Or visit their website at:
  www.lymphoma-action.org.uk

- **Bloodwise** – a charity providing support and information about all kinds of blood cancers, including lymphoma. Their website address is:

  https://bloodwise.org.uk

If you decide you would like to take part then please read and sign the consent form. You will be given a copy of this information sheet and signed consent form to keep. You can have more time to think this over if you are unsure or have more questions.

Local Site Contacts

If you have any questions, please do not hesitate to discuss any questions with your study doctor or members of the study team:

Your study doctor is:

Name: Contact phone number:

Your study/specialist nurse/trial co-ordinator is:

Name: Contact phone number:

Your hospital's Patient Advice and Liaison Service (PALS):

Contact phone number:

Appendix 1: Glossary

Abbreviation	Full Name	What it means
	Biomarker	A substance found in the body which may give information about the cancer prognosis or predict response to a drug.
CT scan	Computer Tomography	Using x-rays to create a 3D picture of inside the body. The image produced is very detailed.
ECG	Electrocardiogram	A test that measures the electrical impulses that make your heart beat.
IRAS	Integrated Research Application System	An online system used in the UK to obtain permission to carry out health research. Each approved study is given a unique IRAS number.
I.V.	Intravenous	Drugs administered into a vein are administered intravenously. Many chemotherapy drugs are given this way.
MRI scan	Magnetic Resonance Imaging scan	Using a magnetic field to create a picture of inside the body. This is very useful for telling the difference between muscle, soft tissue and bone.
PET scan	Positron Emission Tomography scan	Uses a small amount of radioactive substance to track how the body uses its food source, glucose. This creates a detailed 3D picture of inside the body, and can show how well internal organs are working.
PET-CT scan	Positron Emission Tomography/Computer Tomography scan	A scan which combines both PET scanning and CT scanning as described above.
UCL	University College London	This is the organisation that takes responsibility for the running of the study, known as the Sponsor.
UCL CTC	UCL Cancer Trials Centre	The organisation centrally carrying out the day to day work on the study.

Appendix 2: Possible side effects of Nivolumab

We will be monitoring you closely for side effects, and we will give you treatment to help prevent or reduce them. The following side effects have been reported in previous clinical trials of nivolumab:

Very common (may affect more than 1 in 10 people or >10%)

- Diarrhoea (watery, loose or soft stools)
- Fatigue
- Itching
- Rash

Common (may affect between 1 in 100 to 1 in 10 people or 1-10%)

- Abdominal pain
- ~~Cramping~~
- ~~Blood in the stool~~
- Alkaline phosphatase increased (lab test result associated with liver or bone abnormalities)
- ALT increased (lab test associated with abnormal liver function)
- Amylase increased (lab test result associated with pancreas inflammation)
- AST increased (lab test associated with abnormal liver function)
- Chills
- Colitis (symptoms include abdominal pain, cramping, diarrhoea and blood in the stool)
- Constipation
- Cough
- Creatinine increased (lab test result associated with decreased kidney function)
- Decreased appetite
- Dizziness
- Dry mouth
- Dry skin
- Fever
- Headache
- Increased blood sugar
- Inflammation of the colon
- Inflammation of the mouth
- Infusion related reaction
- Joint pain or stiffness
- Lipase increased (lab test result associated with pancreas inflammation)
- Loss of colour (pigment) from areas of the skin
- Lung inflammation (pneumonitis)
- Musculoskeletal pain
- Nausea
- Redness
- Shortness of breath
- Low sodium levels in the blood
- Swelling, including face, arms and legs
- Thyroid gland function decreased
- Thyroid gland function increased
- Thyroid stimulating hormone increased (lab test result associated with abnormal thyroid function)
- Vomiting

Uncommon (may affect between 1 in 1,000 to 1 in 100 people or 0.1-1%)

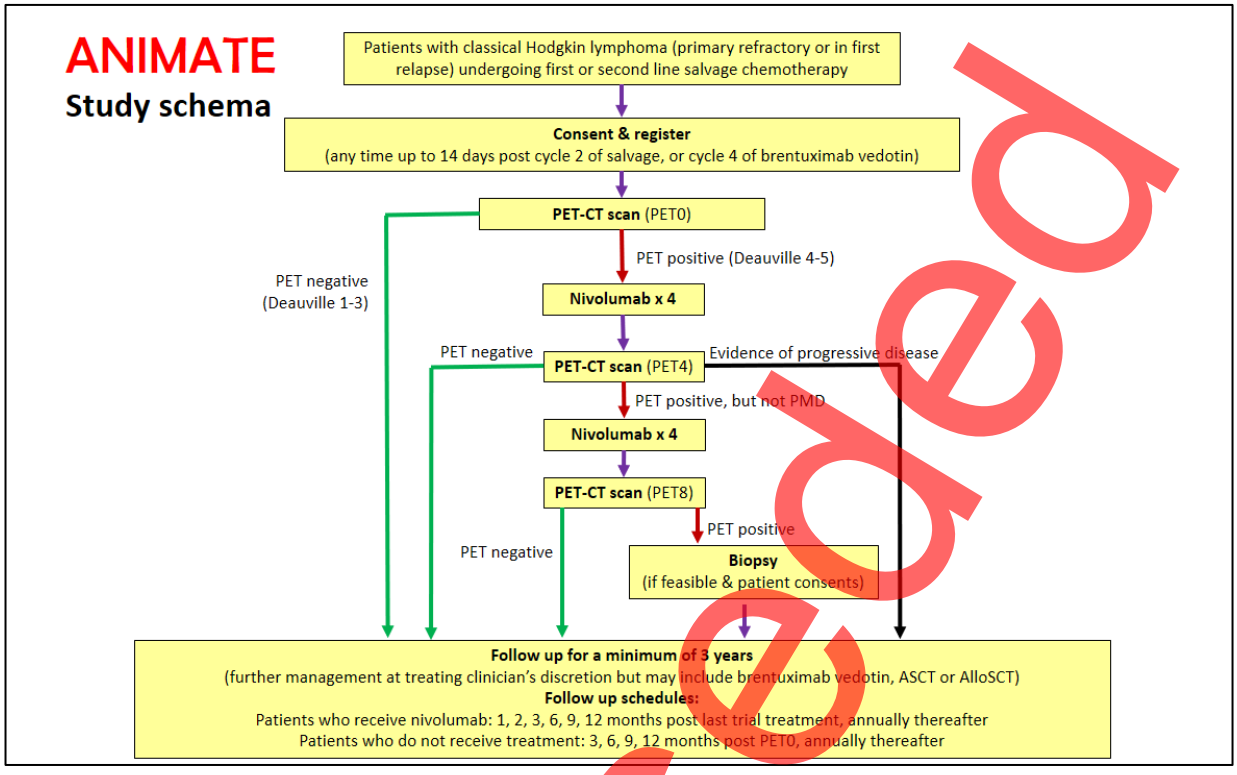
- Adrenal gland function decreased
- Allergic reaction/hypersensitivity
- Bilirubin increased (liver function blood test)
- Bronchitis
- Cranial nerve disorder
- Diabetes
- Dry eyes
- Hair loss
- Heart rate increased
- Heart rhythm abnormal
- High blood pressure
- Hives
- Inflammation of the eye
- Inflammation of the kidney
- Inflammation of the pancreas
- Inflammation of the pituitary gland
- Inflammation of the stomach
- Inflammation of the thyroid gland

- Liver inflammation
- Low blood pressure
- Lung infiltrates, associated with infection or inflammation
- Pituitary gland function increased
- Psoriasis: characterised by patches of abnormal, scaly skin
- Renal (kidney) failure or kidney injury
- Respiratory failure
- Upper respiratory tract infection
- Vertigo (feeling off balance which can lead to dizziness)
- Vision blurred

Rare (may affect between 1 in 10,000 to 1 in 1000 people or 0.01%-0.1%)

- Anaphylactic reaction (severe allergic reaction)
- Damage to the protective covering of the nerves in the brain and spinal cord
- Diabetes complications resulting in excess blood acids an diabetic coma
- Erythema multiforme: skin inflammatory reaction
- Guillan-Barré syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
- Inflammation of the blood vessels
- Inflammation in the brain, potentially life-threatening or fatal
- Inflammation of the heart
- Muscle inflammation
- Myasthenic syndrome (neurological condition characterised by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of the eye, face, breathing and swallowing muscles
- Polymyalgia rheumatica, an inflammatory disorder causing muscle pain and stiffness
- Rhabdomyolysis: muscle fibre released into the blood stream, which could damage your kidneys
- Rosacea: an acne-like skin condition resulting in redness of the face
- Sarcoidosis: a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as the lungs, skin and lymph nodes
- Stevens-Johnson syndrome: an inflammatory disorder of the skin and mucous membranes, resulting in blistering and shedding of skin
- Toxic epidermal necrolysis: a potentially fatal disease characterised by blistering and peeling of the top layer of skin resembling a severe burn
- Histiocytic necrotising lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which cases the lymph nodes to become enlarged, inflamed and painful, commonly affecting lymph nodes of the neck and possibly associated with fever or muscle and joint pains
- Vogt Koyanagi Harada syndrome: a disease that affects the pigmented tissue. This may affect the eye leading to swelling, pain and/or blurred vision; the ear leading to hearing loss, ringing in the ears and/or the skin leading to loss of skin colour

Appendix 3: Summary of the ANIMATE patient treatment pathway



Appendix 4: Summary of tests performed for the ANIMATE trial

Visit	Standard tests	Extra tests for trial
Screening	• None	• Medical history • Pregnancy test (women of childbearing potential only)
After 2 cycles of 1st or 2nd line salvage (or 3/4 cycles of Brentuximab Vedotin)	• PET-CT scan • Clinical examination • Blood counts • Blood chemistry • Weight	• Contrast enhanced CT scan • Heart function tests • Lung function test • Hepatitis B & C testing (additional tests done on the blood samples you have as standard) • • Thyroid function tests (additional tests done on the blood samples you have as standard) • ~~Tests of hormone levels (additional tests done on the blood samples you have as standard)~~Tests for autoimmune conditions (additional tests done on the blood samples you have as standard) • Pregnancy test (women of childbearing potential only)
Before cycle 1	• Clinical examination • Blood counts • Blood chemistry	• Blood sample (55ml) to be sent to central laboratory • Oxygen saturation • Pregnancy test (women of childbearing potential only)
Before cycle 2	• Clinical examination • Blood counts • Blood chemistry	• Blood sample (25ml) to be sent to central laboratory • Oxygen saturation ~~Tests for autoimmune conditions (additional tests done on the blood samples you have as standard)~~
Before cycle 3	• Clinical examination • Blood counts • Blood chemistry	• Pregnancy test (women of childbearing potential only) • Oxygen saturation Thyroid function tests (additional tests done on the blood samples you have as standard) • • ~~Tests for autoimmune conditions (additional tests done on the blood samples you have as standard)~~
Before cycle 4	• Clinical examination • Blood counts • Blood chemistry	• Blood sample (25ml) to be sent to central laboratory • ~~Thyroid function tests (additional tests done on the blood samples you have as standard)~~ • Oxygen saturation

		• ~~Tests for autoimmune conditions (additional tests done on the blood samples you have as standard)~~
End of cycle 4	• None	• PET-CT scan • Contrast enhanced CT scan • Lung function tests (if PET negative or progressive disease)
Before cycle 5	• Clinical examination • Blood counts • Blood chemistry	• Pregnancy test (women of childbearing potential only) • Oxygen saturation • Tests for autoimmune conditions (additional tests done on the blood samples you have as standard) • Thyroid function tests (additional tests done on the blood samples you have as standard)
Before cycle 6	• Clinical examination • Blood counts • Blood chemistry	• Blood sample (25ml) to be sent to central laboratory • Oxygen saturation • ~~Tests for autoimmune conditions (additional tests done on the blood samples you have as standard)~~
Before cycle 7	• Clinical examination • Blood counts • Blood chemistry	• Pregnancy test (women of childbearing potential only) • Thyroid function tests (additional tests done on the blood samples you have as standard) • Oxygen saturation • ~~Tests for autoimmune conditions~~
Before cycle 8	• Clinical examination • Blood counts • Blood chemistry	• Blood sample (25ml) to be sent to central laboratory • Oxygen saturation ~~Tests for autoimmune conditions (additional tests done on the blood samples you have as standard)~~
End of cycle 8	• None	• PET-CT scan • Contrast enhanced CT scan • Lung function test • Repeat tumour biopsy to be sent to central laboratory (optional; if PET positive)
1 month after treatment	• Clinical examination • Blood counts • Blood chemistry	• Blood sample (25ml) to be sent to central laboratory • Tests for autoimmune conditions (additional tests done on the blood samples you have as standard) • Thyroid function tests (additional tests done on the blood samples you have as standard) • Pregnancy test (women of childbearing potential only)

2 months after treatment	• Clinical examination • Blood counts • Blood chemistry	• Tests for autoimmune conditions (additional tests done on the blood samples you have as standard) • Thyroid function tests (additional tests done on the blood samples you have as standard) • Pregnancy test (women of childbearing potential only)
3 months after treatment	• Clinical examination • Blood counts • Blood chemistry	• Tests for autoimmune conditions (additional tests done on the blood samples you have as standard) • Thyroid function tests (additional tests done on the blood samples you have as standard) • Pregnancy test (women of childbearing potential only)
6 months after treatment	• Clinical examination • Blood counts • Blood chemistry • Remission status assessment (investigations as per local policy	• Assessment for late toxicity of nivolumab
9 months after treatment	• Clinical examination • Blood counts • Blood chemistry • Remission status assessment (investigations as per local policy	• Assessment for late toxicity of nivolumab
12 months after treatment	• Clinical examination • Blood counts • Blood chemistry • Remission status assessment (investigations as per local policy	• Assessment for late toxicity of nivolumab • Lung function test
~~1 year after treatment~~	~~• Clinical examination~~ ~~• Blood counts~~ ~~• Blood chemistry~~	~~• Lung function test~~