

*To be printed on local hospital headed paper*



**Patient Information Sheet**

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| **Study Title: An open label phase II trial of temozolomide prior to nivolumab in MGMT methylated, advanced oesophagogastric cancer****Researcher: Dr Elizabeth Smyth****ERGO Ref: 61191****IRAS: 282284** |

**You are being invited to take part in the above research study. To help you decide whether you would like to take part or not, it is important that you understand why the research is being done and what it will involve. Please read the information below carefully and ask questions if anything is not clear or you would like more information before you decide whether to take part in this research. You may like to discuss it with others, but it is up to you to decide whether or not to take part. If you are happy to participate you will be asked to sign a consent form.**

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| **Contents**Part A – pages 2 to 8 - describes the purpose of this study and what will happen to you if you take part.Part B – pages 8 to 12 - gives detailed information about the conduct of the study and important contact details. |  | **How to contact us**If you have any questions about this trial or would like to discuss it further, please contact:[local investigator name][contact details] |

**Do I have to take part?** No. It is entirely up to you if you take part in the trial or not. If you choose not to take part, the care you get from your own doctors will not be affected in any way.

**If I start the trial, can I stop if I want to?** Yes. If you choose to take part in the trial, you are free to stop treatment at any point without giving a reason – the standard of your care will not be affected.

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| **Important things you need to know*** The ELEVATE trial is open to patients with advanced oesophageal cancer, whose tumours have been identified as methylated in a specific enzymatic protein i.e. MGMT (methylguanine-deoxyribonucleic acid methyltransferase)
* The aim of this trial is to determine the activity and safety of the chemotherapy drug Temozolomide (TMZ) plus an immunotherapy drug i.e. Nivolumab (NIVO).
* The response rate of the medication on the tumour (how much the tumour shrinks) will be measured.
* You will need to sign a consent form before taking part in the trial to confirm that you understand it and agree to take part.
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**Part A: The reasons for this study and what is involved**

**What is the research about?**

Patients with advanced or metastatic oesophagogastric cancer cannot be cured with current treatments and do not have good survival outcomes compared to other cancers. We are investigating whether chemotherapy treatment with temozolomide (TMZ) plus nivolumab (NIVO) an immunotherapy drug that is not currently licensed in Europe for oesophagogastric cancer (but is licensed and used in other cancers) will allow patients with MGMT methylated tumours to improve their survival rates. There is evidence from laboratory models and other tumours to show that when TMZ is used in MGMT methylated tumours that the number of mutations (mistakes in DNA [deoxyribonucleic acid]) in the tumour increases. Tumours with high numbers of mutations tend to respond better to immunotherapy like nivolumab (NIVO). It is hoped that MGMT methylated tumours will become sensitive to nivolumab, by treating them with TMZ, which could lead to tumour shrinkage. The trial is being sponsored by the University of Southampton.

**Why have I been asked to participate?**

You have been invited to take part because you have been diagnosed with advanced, previously treated and currently unresectable (inoperable) oesophagogastric cancer that is methylated in MGMT (enzymatic protein) and have been treated with 3-6 months of first line chemotherapy. Your medical team feel that this trial may be of interest to you. The trial is aiming to recruit 18 patients in total.

**How will my treatment be decided?**

Everyone who agrees and is suitable will receive the same treatment if they stay on the trial. Initially you will receive a metronomic TMZ dose. Metronomic dose is when the chemotherapy treatment is given in low doses on a continuous schedule (in this case daily), usually over a long time. In the trial you will have TMZ for up to 3 months. You will then either have nivolumab as well as TMZ or if the TMZ has stopped working (your tumour grows) before 3 months you will just start nivolumab on its own. This is explained in a diagram below.



**What will happen to me if I take part?**

Following consent, you will undergo screening to ensure that this trial is right for you. Once screened eligible you will start the TMZ. TMZ is a capsule that you will take every day for up to 3 months. During treatment with TMZ, you will have weekly blood tests and every 4 weeks a clinic visit to monitor your health and have a physical examinations. If your disease progresses whilst on TMZ you will stop that treatment and receive nivolumab treatment. If your disease doesn’t progress (grow) on TMZ, you will start NIVO at 3 months and continue with TMZ as well. You will visit the clinic every 2 weeks during nivolumab treatment to be monitored for health and progression. The nivolumab treatment will be given via an infusion (injected into a vein). At regular intervals you will have CT scans (computerised tomography scan) to monitor the effect of the treatment. These are the same as what you would have normally to monitor your well-being although one would be additional to your standard of care. To ensure that your heart is well enough to receive the treatment you will also have either an echocardiogram or a MUGA scan (multigated acquisition scan). At 3 months or when the TMZ treatment is stopped you will undergo an endoscopy. During the endoscopy a biopsy will be taken at this time – you will not be asked to undertake an additional procedure to acquire the biopsy, if you have the endoscopy. We will also ask you to have one at the end of nivolumab treatment – but this one would be optional. Following progression (growth of your tumour) of disease on nivolumab, you will move into the follow up phase of the trial to monitor for overall survival.

We will ask you to give your consent for up to 5 additional blood samples; one at the start of the trial and the others during the treatment.

A schedule of visits and activities to be conducted at these visits can be found at the end of this document for reference.

**Expenses and Payment**

You will not receive any payment for taking part in this trial, nor will your travel expenses be reimbursed.

**What are the possible benefits, risks, and disadvantages of taking part?**

* You may benefit from a longer period of disease remission by having the combination treatment of TMZ followed by nivolumab. However, this cannot be guaranteed and there may be no additional benefit for you in relation to how long your cancer is controlled.
* The information that we get from this study may help us to treat future patients with the same condition in a more effective way.
* The inconvenience, side effects and impact on quality of life is similar to that of any course of chemotherapy and immunotherapy.
* You will be helping to further our knowledge of how to treat cancer and this will also benefit society as a whole.

Radiation Risks

* During the trial, you will have contrast enhanced CT scans to assess your cancer. These tests use radiation, which has a limited increase to your risk of cancer in the future. These tests are part of standard care but you will receive one additional scan by taking part in the trial.
* You will also be required to have an echocardiogram or MUGA, depending on your hospital’s practice, to ensure you are well enough to receive the full dose of chemotherapy.

**Risk Explanations:**

A **contrast enhanced CT scan** involves radiation, using X-Rays to get a detailed image of the body area. If you take part in this study, you will have up to 10 CT scans of your chest+abdomen+pelvis. You may also have a nuclear medicine **MUGA** scan to assess your heart function. Some of these 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 or provide your doctor with other clinical information. Ionising radiation can cause cell damage that may, after many years or decades, turn cancerous. In patients with your current clinical condition, the chance of this happening to you is extremely small.

**What are the side effects of the treatments?**

Treatments for cancer often have side effects, including some that are life-threatening. There may be additional unknown risks.

If you experience severe side effects associated with the study drug, your doctor may prescribe medications to treat the side effect(s), future treatments may be delayed, or treatment may be stopped permanently. Any significant new findings that develop during the course of the research and which may relate to your willingness to continue participation, will be provided to you.

*Contact your doctor immediately if you have any of the following:*

A severe allergic (hypersensitive) reaction (hives, wheezing or other breathing difficulty), uncontrolled bleeding, seizures (convulsions), fever, chills, severe headache that does not go away.

**Side effects specific to temozolomide**

**Very common (may affect more than 1 in 10 people)**

* Anorexia
* Convulsions, weakness on one side of the body (hemiparesis), aphasia/ dysphasia (difficulty communicating), headache
* Diarrhoea, constipation, nausea, vomiting
* Rash, Alopecia (hair loss)
* Fatigue

**Common (may affect up to 1 in 10 people)**

* Infections, shingles (herpes zoster), sore throat (pharyngitis), oral thrush (candidiasis oral)
* A reduction in certain kinds of blood cells which may cause you to have increased bruising or bleeding, anaemia (a shortage of red blood cells), fever, and reduced resistance to infections. The reduction in blood cell counts is usually short-lived. In some cases, it may be prolonged and may lead to a very severe form of anaemia (aplastic anaemia)
* Allergic reaction
* Excess cortisol which can lead to facial puffiness and weight gain (Cushingoid)
* Agitation, amnesia, depression, anxiety, confusion, insomnia
* Ataxia (balance impaired), cognition impaired, concentration impaired, consciousness decreased, dizziness, hypoesthesia (loss of sensation), memory impaired, neurological disorder, neuropathy, paraesthesia (burning or prickling sensation in hands and feet), somnolence (drowsiness), speech disorder, taste perversion, tremor
* Hemianopia (partial blindness), vision blurred, vision disorder, visual field defect, diplopia (double vision), eye pain
* Deafness, vertigo, tinnitus, earache
* Haemorrhage, pulmonary embolism (blood clot in the lung), deep vein thrombosis, hypertension (high blood pressure)
* Pneumonia, dyspnoea (laboured breathing), sinusitis, bronchitis, coughing, upper respiratory infection
* Stomatitis (inflammation of mouth and lips), abdominal pain, dyspepsia (indigestion), dysphagia (difficulty swallowing)
* Erythema (skin redness), dry skin, pruritus
* Frequent urination, urinary incontinence
* Fever, influenza-like symptoms, asthenia (lack of energy), malaise, pain, oedema and oedema peripheral
* Elevation of liver enzymes, fluctuations in weight

**Uncommon (may affect up to 1 in 100 people)**

* Opportunistic infection sepsis, meningoencephalitis herpetic, CMV (cytomegalovirus) infection, CMV reactivation, hepatitis B virus, herpes simplex, infection reactivation, wound infection, gastroenteritis
* Abnormalities of blood cells.
	+ Myelodysplastic syndrome (MDS), secondary malignancies, including myeloid leukaemia
	+ Prolonged deficiency of red and white blood cells and platelets (pancytopenia), aplastic anaemia, petechiae (bleeding under skin)
* Severe allergic reaction: Anaphylaxis
* Hypokalaemia (potassium deficiency), increased alkaline phosphatase
* Behaviour disorder, emotional lability, hallucination, apathy
* Prolonged seizures (status epilepticus), hemiplegia (weakness/stiffness in one side of the body), extrapyramidal disorder (involuntary movements), parosmia (affecting sense of smell), hyperaesthesia (physical sensitivity), sensory disturbance, abnormal coordination and gait
* Difficulty seeing (Visual acuity reduced), dry eyes
* Difficulty hearing (hearing impairment), hyperacusis (when sounds seem louder than they are), otitis media (inflammation of the ear)
* Palpitation (feeling of heart beating fast or irregularly).
* Cerebral haemorrhage, flushing, hot flushes
* Difficulty breathing: Respiratory failure, interstitial pneumonitis/pneumonitis (inflammation of the lung), pulmonary fibrosis, nasal congestion
* Abdominal distension, faecal incontinence, gastrointestinal disorder, haemorrhoids, dry mouth
* Liver injury: Hepatic failure, hepatic injury, hepatitis, cholestasis, hyperbilirubinemia, Gamma-glutamyltransferase increased
* Skin rashes which could be severe: oxic epidermal necrolysis, Stevens-Johnson syndrome, angioedema, erythema multiforme, erythroderma, skin exfoliation, photosensitivity reaction, urticaria, exanthema, dermatitis, sweating increased, pigmentation abnormal
* Pain on passing urine: Dysuria
* Menstrual changes (vaginal haemorrhage, menorrhagia, amenorrhoea, vaginitis), breast pain, impotence
* Condition aggravated, rigors, face oedema, tongue discolouration, thirst, tooth disorder

**Side effects specific to nivolumab**

**Be aware of important symptoms of inflammation.** Nivolumab acts on your immune system and may cause inflammation in parts of your body. Inflammation may cause serious damage to your body and some inflammatory conditions may be life-threatening and need treatment or withdrawal of nivolumab.

The following side effects have been reported **with nivolumab alone:**

**Very common (may affect 1 in 10):**

* Diarrhoea
* Feeling tired or lack of energy
* Skin itching
* Skin rash

**Common (may affect between 1 in 100 to 1 in 10):**

* Abdominal pain
* Alkaline phosphatase increased: lab test result associated with liver or bone abnormalities
* Allergic reaction/hypersensitivity
* ALT increased: lab test result associated with abnormal liver function
* Amylase increased: lab test result associated with pancreas inflammation
* AST increased: lab test result associated with abnormal liver function
* Bilirubin increased: lab test result associated with abnormal liver function
* Chills, Constipation, Cough
* Creatinine increased: lab test result associated with decreased kidney function
* Decreased appetite
* Dizziness or vertigo (feeling off balance which can lead to dizziness)
* Dry mouth, dry skin
* Fever, headache, increased blood sugar
* Inflammation of the colon
* Inflammation of the mouth
* Lipase increased: lab test result associated with pancreas inflammation
* Loss of colour (pigment) from areas of skin
* Low levels of sodium in the blood
* Low platelet counts (thrombocytopenia): this may increase your risk for skin bruising, nose bleeds, and bleeding from the gums
* Low red blood cell counts (anaemia): this may make you feel weak and tired
* Lung inflammation (pneumonitis): it is possible that nivolumab may cause inflammation of the tissues of the lung. This adverse effect has been reported in patients treated with nivolumab. While many patients with X-ray or CT abnormalities have not developed any symptoms, some patients have developed mild to severe symptoms and in rare cases, death has occurred as a result of their lung inflammation. Signs and symptoms of lung inflammation may include difficulty breathing, pain or discomfort while breathing, chest pain, cough, shortness of breath, increased rate of breathing, fever, low blood oxygen levels, or fatigue
* Nausea, vomiting
* Pain in the muscles, bones, ligaments, tendons, and nerves
* Reaction related to infusion of the medicine. The symptoms may include but not limited to fever, rash, pain, swelling
* Redness of skin
* Shortness of breath
* Swelling, including face, arms, and legs (oedema)
* Thyroid gland function decreased or may be increased; increased thyroid stimulating hormone - a lab test result associated with abnormal thyroid function
* Tingling, burning, numbness or weakness, possibly in arms, legs, hands and feet

**Uncommon (may affect between 1 in 100 to 1 in 1,000):**

* Bronchitis: inflammation of the lining of bronchial tubes, which carry air to and from the lungs
* Low white blood cell counts (neutropenia): these put you at higher risk for infection
* Decreased secretion of hormones produced by adrenal glands
* Decreased thyroid stimulating hormone - a lab test result associated with abnormal thyroid function
* Dehydration
* Diabetes: a disease that results in too much sugar in the blood
* Dry eye
* Erythema multiforme: a skin disorder that's considered to be an allergic reaction to medicine or an infection. Symptoms may include symmetrical, red, raised skin areas that can appear all over the body, more noticeable on the fingers and toes. These patches often look like "targets" (dark circles with purple-grey centers)
* Hair loss
* Heart rate increased or abnormal heart rhythm
* High blood pressure
* Hives
* Inflammation of the eye, kidney, pancreas, pituitary gland, stomach, thyroid gland, liver
* Joint pain or stiffness
* Kidney function failure, kidney disease
* Low blood pressure
* Pemphigoid: blistering of the skin or mouth caused by the immune system attacking healthy tissue
* Respiratory failure: a condition in which not enough oxygen passes from your lungs into your blood, or when your lungs cannot properly remove carbon dioxide
* Skin disease with thickened patches of red skin, often silvery scales (Psoriasis)
* Trouble falling and/or staying asleep (Insomnia)
* Underactive function of the pituitary gland situated at the base of the brain
* Upper respiratory tract infection: a common viral / bacterial infection that affects the nose, throat, and airways
* Vision blurred

**Rare (may affect 1 in 1,000 to 1 in 10,000):**

* Autoimmune hemolytic anaemia: a malfunction of the immune system that produces autoantibodies, which attack red blood cells as if they were foreign substances to the body
* Cranial nerve disorder
* Damage to the protective covering of the nerves in the brain and spinal cord
* Diabetes complications resulting in excess blood acid
* Disease caused by the body’s immune system attacking healthy organs
* Double vision
* Drug induced liver injury
* Guillain-Barre syndrome, an autoimmune disorder associated with progressive muscle weakness or paralysis
* Histiocytic necrotizing lymphadenitis or Kikuchi lymphadenitis: disorder of the lymph nodes which causes 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
* Inflammation including that of the blood vessels, the brain, potentially life-threatening or fatal, the heart, the lining of the brain and spinal cord
* Lung infiltrates, associated with infection or inflammation
* Muscle inflammation
* Myasthenic syndrome (neurologic syndrome characterized by muscle weakness) including myasthenia gravis, a nerve disease that may cause weakness of eye, face, breathing, and swallowing muscles
* Pericarditis: a swelling and irritation of the thin saclike membrane surrounding the heart (pericardium)
* Polymyalgia rheumatica: an inflammatory disorder that causes muscle pain and stiffness, especially in the shoulders
* Rhabdomyolysis: muscle fibre released into the blood stream which could damage your kidneys
* Rosacea: acne-like skin condition resulting in redness of face
* Rupture of the intestine/hole in the intestine
* Sarcoidosis: a disease involving abnormal collections of inflammatory cells (granulomas) in organs such as lungs, skin, and lymph nodes
* Severe allergic reaction may include but not limited to high grade fever, rash, swelling and pain
* Stevens Johnson syndrome: inflammatory disorder of skin and mucous membranes, resulting in blistering and shedding of skin
* Toxic epidermal necrolysis: a potentially fatal disease characterized by blistering and peeling of the top layer of skin resembling a severe burn

**Contraception and pregnancy during the trial.**

Women

If you are pregnant or breast feeding, you will not be able to enter the ELEVATE trial. Women who can bear children must agree to use two forms of contraception – one of which should be highly effective or abstinence during the study and for 5 months after the last dose of trial drug and will need to have a negative pregnancy test at screening (prior to starting treatment).

* Methods that are considered highly effective include oral, intravaginal or transdermal combined (oestrogen and progesterone containing) hormonal contraception; oral, injected or implanted progesterone only hormonal contraception; an intra-uterine device; intrauterine hormone-releasing system (IUDS); bilateral tubal occlusion; vasectomised partner.
* Methods that are considered effective include progesterone only oral hormonal contraception (where inhibition of ovulation is not the primary mode of action); male or female condom; cap; diaphragm or sponge with spermicide.

Please be aware that if you become pregnant during the trial, you will not be able to continue taking part in the trial. Highly effective contraception options will be discussed with you by your study doctor.

You must refrain from any egg donation from the start of your trial treatment, throughout the trial and for 5 months after finishing treatment.

Men

If your partner is pregnant or breast-feeding, we advise you to use barrier method contraception to make sure that the baby is not exposed to the trial drug. If you have a partner of child bearing potential, you must agree to use two forms of contraception from the start of your trial treatment, one of which should be highly effective, throughout the trial and for 7 months after finishing treatment.

* Methods that are considered highly effective include oral, intravaginal or transdermal combined (oestrogen and progesterone containing) hormonal contraception; oral, injected or implanted progesterone only hormonal contraception; an intra-uterine device; intrauterine hormone-releasing system (IUDS); bilateral tubal occlusion; vasectomy.
* Methods that are considered effective include progesterone only oral hormonal contraception (where inhibition of ovulation is not the primary mode of action); male or female condom; cap; diaphragm or sponge with spermicide.

You must refrain from any sperm donation from the start of your trial treatment, throughout the trial and for 7 months after finishing treatment. Highly effective contraception options will be discussed with you by your study doctor.

**Future fertility** – chemotherapy can affect your ability to have children in the future so, you may wish to discuss this, and the possibility of storing eggs/sperm, with your doctor.

**What data will be collected?**

We will be using information from you and your medical records in order to undertake this study. Research staff at your treating hospital will enter the data relating to your disease and the trial treatment onto an electronic database. The data will be identified by your unique trial ID number only. The Southampton Clinical Trials Unit are responsible for looking after your information and using it properly. They will keep your non-identifiable research data for 25 years after the study has finished.

Non-identifiable data, managed by the Southampton Clinical Trials Unit, will be held on the online clinical trial database software Medidata Rave. This software is hosted on secure servers in the EU and the US. Access to this data will be strictly controlled by the Southampton Clinical Trials Unit and no third parties will be granted access to the Medidata servers holding your research data. All applicable Data Protection legislation will be obeyed by the University of Southampton.

Your data will be pseudo-anonymised in order to protect your identity; this means the data will undergo a de-identification procedure where your personal identifiable data (e.g. name, full date of birth) are replaced with one or more artificial identifiers. Therefore, you will be referred to solely as this unique reference number for the duration of the trial.

**What will happen to the samples I give?**

The blood samples will be sent to the MRC Cancer Unit at the University of Cambridge for central analyses. All the samples that you provide as part of the study would be anonymised so that it would not be possible to identify you. Part of your samples may also be used in future ethically approved studies.

**Will any genetic tests be done?**

The study will take blood samples to perform genetic analyses that may help in the research of identifying more effective treatments in patients with advanced oesophagogastric cancer.

Your tumour will be tested for specific mutations which might help tell us which tumour respond better to treatment. However, no genetic testing of non-tumour tissue will be done therefore there will not be any assessment of inherited or familial cancer genes, or genes which might predict for other illnesses.

**What will happen at the end of the trial?**

At the end of the trial you will return to the standard care at your hospital. Your doctor will discuss future care with you.

**Part B: Further information**

**What if new information becomes available?**

Sometimes we get new information about the treatment being studied. If this happens and it affects your participation in the study, your doctor will discuss the information with you. If, on the basis of this information, you decide not to continue with the study, your doctor will make arrangements for your continued care. If you decide to continue in the study, you may be asked to sign another consent form. It may be that your doctor feels that you should withdraw from the study. If this happens, they will arrange for further treatment if required. If the study is stopped for any reason, you will be informed and further care arranged.

**What happens if something goes wrong?**

If you have a concern about any aspect of this study, you should contact your research doctor/nurse as soon as possible. Your clinical research team will do their best to help you and answer your questions. [Insert site phone number].

If you wish to complain, or have any concerns about the way you have been approached or treated during this trial, the normal complaints system will be available to you; this service is called the Patients Advice and Liaison Service (PALS) in England and Wales. The service available to patients in Scotland is the Health Boards Complaints Team. For the contact details and further information please check [www.nhs.uk](file:///%5C%5Csoton.ac.uk%5Cresource%5CMedicine%5CCTU%5CTrials%5C07%20Trials%20in%20development%20for%20submission%5COELIXIR%20TRIALS%5C1.%20CRUK%20APPLICATION%202019%5C3a%20Rise%5Cwww.nhs.uk%20) or your local trust’s website.

[Delete as appropriate]

Local PALS contact details [insert here]

Local Health Boards Complaints Team contact details [insert here]

The study Sponsor, University of Southampton, takes overall responsibility for the trial. If you remain unhappy or have a complaint about any aspect of this study, please contact the University of Southampton Research Integrity and Governance Manager (023 8059 5058, rgoinfo@soton.ac.uk).

Please be aware that if you are harmed as a result of taking part in the ELEVATE trial, there are no special compensation arrangements. The University of Southampton provides clinical trials indemnity insurance for negligence in its management or design of the trial. If you are harmed because of someone’s negligence, you may be able to take legal action, but you may have to pay your own legal costs

**Will my participation be kept confidential?**

Yes. Your participation and the information we collect about you will be kept strictly confidential. Your GP will be informed of your participation in the ELEVATE trial.

Research Data

We will be using information from you and your medical records in order to undertake this study. We are responsible for looking after your information and using it properly. The Southampton Clinical Trials Unit will keep your non-identifiable research data for 25 years after the study has finished.

In order to properly manage your data and ensure the research is reliable and accurate, your rights to view, change or move the research information we collect about you are limited. You can find out more about how we use your information on the Southampton Clinical Trials Unit website at <https://www.southampton.ac.uk/ctu/about/index.page> or you can contact the Southampton Clinical Trials Unit on 023 8120 5154 and ask to speak to the ELEVATE team.

Your clinician’s research team will collect information from you and your medical records for this research study in accordance with our instructions. Only members of the research team at your NHS Trust and responsible members of the University of Southampton may be given access to data about you for monitoring purposes and/or to carry out an audit of the study to ensure that the research is complying with applicable regulations. Individuals from regulatory authorities (people who check that we are carrying out the study correctly) may look at your medical and research records to check the accuracy of the research study. All of these people have a duty to keep your information strictly confidential.

Your NHS Trust will keep identifiable information about you from this study for 25 years after the study has finished.

Consent Forms

A copy of your consent form, containing your name and initials, will be sent to the Southampton Clinical Trials Unit for confirmation of your consent. This form will be kept securely, as detailed above, for the duration of the trial.

Data Protection Privacy Notice

See *Addendum 1* for information regarding the University of Southampton’s Data Protection Privacy Notice.

**Impact on Insurance**

Participation in any research study has the potential to impact any insurance cover that you may have (e.g. travel insurance, protection insurance  (life insurance, income protection, critical illness cover) and private medical insurance) and it is advised that you seek expert advice on these issues, where necessary.

**NHS Digital**

NHS Digital collects data from across health and social care in the England and there are equivalents in the other devolved nations. With your consent, During the trial, NHS Digital, or the applicable service in your area, may provide certain information about your health status to the University of Southampton Clinical Trials Unit (CTU) upon request. The University of Southampton CTU is registered under the Data Protection Regulations to hold such information on a confidential basis.

**Do I have to take part?**

No, it is up to you to decide to join the study. We will describe the study in detail and go through this information sheet with you. If you agree to take part, we will ask you to sign a consent form with the doctor. You are free to withdraw at any time, without giving us a reason. Your withdrawal from the study will not affect the standard of care that you will receive in any way.

**What happens if I change my mind?**

You have the right to change your mind and withdraw at any time without giving a reason and without your participant rights (or routine care if a patient) being affected.

**What will happen to the results of the trial?**

At the end of the trial, any results will be analysed and presented at national or international meetings and will also be published in a medical journal. Your personal details will remain strictly confidential. Research findings made available in any reports or publications will not include information that can directly identify you without your specific consent.

**Who is organising and funding the trial?**

The trial is being coordinated by the Southampton Clinical Trials Unit. The trial is being funded by Bristol Myers Squibb. The Sponsor is University of Southampton. The study has been ethically reviewed by the East of England – Cambridge South Research Ethics Committee and regulatory reviewed by the Medicines and Healthcare products Regulatory Agency (MHRA).

**Where can I get more information?**

If anything is unclear regarding this study information, please contact:

[Named site nurse] Research nurse, [insert site name] on Tel [……]

Dr [insert name site] PI, [insert PI name], Tel [insert number site specific]

In an **EMERGENCY**, please contact:

[Insert site-specific contact details]

**Addendum 1 - Data Protection Privacy Notice**

The University of Southampton conducts research to the highest standards of research integrity. As a publicly-funded organisation, the University has to ensure that it is in the public interest when we use personally-identifiable information about people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use information about you in the ways needed, and for the purposes specified, to conduct and complete the research project. Under data protection law, ‘Personal data’ means any information that relates to and is capable of identifying a living individual. The University’s data protection policy governing the use of personal data by the University can be found on its website (https://www.southampton.ac.uk/legalservices/what-we-do/data-protection-and-foi.page).

This Participant Information Sheet tells you what data will be collected for this project and whether this includes any personal data. Please ask the research team if you have any questions or are unclear what data is being collected about you.

Our privacy notice for research participants provides more information on how the University of Southampton collects and uses your personal data when you take part in one of our research projects

and can be found at: <http://www.southampton.ac.uk/assets/sharepoint/intranet/ls/Public/Research%20and%20Integrity%20Privacy%20Notice/Privacy%20Notice%20for%20Research%20Participants.pdf>

Any personal data we collect in this study will be used only for the purposes of carrying out our research and will be handled according to the University’s policies in line with data protection law. If any personal data is used from which you can be identified directly, it will not be disclosed to anyone else without your consent unless the University of Southampton is required by law to disclose it.

Data protection law requires us to have a valid legal reason (‘lawful basis’) to process and use your Personal data. The lawful basis for processing personal information in this research study is for the performance of a task carried out in the public interest. Personal data collected for research will not be used for any other purpose.

For the purposes of data protection law, the University of Southampton is the ‘Data Controller’ for this study, which means that we are responsible for looking after your information and using it properly. The University of Southampton will keep identifiable information about you for 25 years after the study has finished after which time any link between you and your information will be removed.

[NHS/ other site] will keep identifiable information about you from this study for 25 years after the study has finished.

To safeguard your rights, we will use the minimum personal data necessary to achieve our research study objectives. Your data protection rights – such as to access, change, or transfer such information - may be limited, however, in order for the research output to be reliable and accurate. The University will not do anything with your personal data that you would not reasonably expect.

If you have any questions about how your personal data is used, or wish to exercise any of your rights,

please consult the University’s data protection webpage:

(https://www.southampton.ac.uk/legalservices/what-we-do/data-protection-and-foi.page) where you can make a request using our online form. If you need further assistance, please contact the University’s Data Protection Officer (data.protection@soton.ac.uk).

Thank you for reading this information sheet. If you decide to take part in the study, you must personally initialise, sign and date a consent form.

We will give you a copy of this information sheet and your signed consent form to keep. We will keep a second copy of this document with the research records on this trial and place a third copy in your hospital records.

**Schedule of trial visits:**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Visit:** | **Screening**  | **Baseline Visit** | **Day 1 of each TMZ cycle** | **At 3 months or end of TMZ treatment** | **Day 1 of each Nivolumab (+/- TMZ) cycle**  | **End of trial treatment** |
| Informed Consent  | X |  |  |  |  |  |
| Eligibility Evaluation | X |  |  |  |  |  |
| Medical History  | X |  |  |  |  |  |
| Physical Exam  | X | X | X | X | X | X |
| Weekly phone call during TMZ treatment (not done on weeks that the patient attends clinic) |  |  | X |  | X |  |
| Echo/MUGA (if clinically indicated) | X |  |  |  |  |  |
| Pregnancy Test (if required) | X | X | X |  | X |  |
| CT Scan  | X |  | X | X | X | X |
| Blood tests (weekly whilst taking TMZ) | X | X | X | X | X |  |
| ECG | X |  |  |  |  |  |
| Quality of Life Questionnaires  |  | X | X | X | X |  |
| Record details of next treatment |  |  |  |  |  | X |
| Tumour Biopsy (endoscopy) |  |  |  | X |  | X (optional) |