[To be printed on local hospital headed paper]

Name of local PI – to be added by site.

DOMENICA STUDY

Randomized phase III trial in MMR deficient endometrial cancer patients comparing chemotherapy alone versus Dostarlimab in first line advanced/metastatic setting.

N° EudraCT: 2021-002124-21

DOMENICA PARTICIPANT INFORMATION SHEET (PIS)

Introduction

You have been invited by your doctor to take part in the "**DOMENICA"** study. This study wants to find out if the study treatment, dostarlimab (a medicine that helps your immune system attack cancer cells) is better at potentially preventing womb/uterus cancer from growing compared to chemotherapy, the current standard of care.

To help you decide if you would like to take part, we have put together this information leaflet explaining why we are doing this study and what it would involve for you.

Please take time to read the information carefully and discuss it with friends and relatives, if you wish. Ask your doctor if there is anything that is not clear or if you would like more information.

Your participation in the research is voluntary. You are totally free to accept or refuse to participate and you don't have to justify your decision. If you do not wish to participate, your decision will not impact the quality or type of care that you will receive outside of the study.

If you agree to participate, you must sign the Informed Consent Form (attached at the end of the document). You will be required to sign and date the consent form in triplicate (one for you, one for your doctor, one for medical records) in the presence of your doctor.

Moreover, even after you have dated and signed this study consent form, you are still free to withdraw from the study at any time and without providing any reasons. During the study, your doctor will provide you with any new information that may affect your decision.

Thank you for reading this information. If you wish to consider taking part, you will be given a copy of this information sheet to keep.

CONTENTS

1 WHAT IS THIS STUDY ABOUT?

1.1 What do I need to know?

- You have been diagnosed with a type of womb/uterus cancer (endometrial cancer) that has either come back again or has spread to other parts of your body. This means your cancer cannot be treated by radiotherapy (X-ray treatment) or surgery. You may have previously had treatment with hormones, but the cancer has come back or spread.

- Chemotherapy, a medicine used to kill cancer cells is sometimes given to treat this type of cancer and is the standard of care. A different class of medicines, called immunotherapies, help your body use its own immune system to fight cancer cells. This type of medicine is thought to help fight womb/uterus cancer.

- The DOMENICA study is aiming to find out whether treating this type of cancer with an immunotherapy (Dostarlimab, see section 1.4) is better than chemotherapy alone.

1.2 Invite to participate

Before you decide to take part in this study, it is important that you understand why the research is being done and what it will involve. Please take the time to read this information sheet carefully. You can discuss this study with other people, such as your family or friends. Your doctors or nurses can go through the information sheet with you and answer any questions that you have. If you decide to participate in this study, you will be asked to complete a consent form. Thank you for taking the time to read this information sheet.

1.3 How is my womb/uterus cancer usually treated?

The current standard of care for womb/uterus cancer that has come back or has spread is a chemotherapy medicine called Paclitaxel and Carboplatin. However sometimes even with this treatment, the cancer can progress (relapse) in some patients which is why it's important to find other treatments to limit the chance of the cancer coming back. One of the treatments recently developed, is an immunotherapy called Dostarlimab.

Patients with womb/uterus cancer are closely monitored by their doctors by CT or MRI scans to see if the cancer is getting bigger, smaller, or spreading to another part of the body. You will undergo CT or MRI scans as a part of this trial, the same as standard of care. There is the potential for two additional scans (outside of standard of care) depending on how you respond to treatment.

1.4 What is "Dostarlimab"?

Dostarlimab is a type of immunotherapy. This type of treatment does not target the cancer directly but helps the immune system of the patient able to recognize, attack and destroy the cancer cells. People who research cancer have found that sometimes the body's own immune system may slow down cancer growth. Sometimes, this natural immune system response stops, and cancer cells send out signals to hide from your immune system response and are not killed. Drugs like dostarlimab work to remove these signals and increase your immune response by stopping the cancer from hiding.

Dostarlimab has already been shown to be effective in patients with womb/uterus cancer who have already progressed after chemotherapy but we don't how effective it is for patients who haven't had chemotherapy yet. It is important to find out if this treatment can be used earlier in the care of patients and if it can be used as an alternative to chemotherapy.

You have been asked to take part in this study as you have advanced womb/uterus cancer that has an abnormality of the DNA repair system, named MMR deficient (or MSI-high). Dostarlimab is already licenced to treat this type of cancer in patients who have progressed after treatment with chemotherapy. This study aims to see how the drug works for patients earlier in their treatment journey and if dostarlimab can help prevent progression of your cancer.

1.5 What is the aim of the study?

The aim of this study is to see if dostarlimab as a single therapy is more efficient at reducing the progression of advanced or metastatic womb/uterus cancer than chemotherapy. If successful, study results could be used to expand the licence of dostarlimab for advanced or metastatic womb/uterus cancer to allow earlier access of the drug as part of standard care for patients.

For example, it could be prescribed for the care of patients with an advanced or metastatic womb/uterus cancer at diagnosis, before chemotherapy which could delay potential relapse.

The DOMENICA study aims to evaluate the effectiveness of dostarlimab, as a new treatment for your cancer.

The study also aims to:

- regularly monitor the side effects which could occur in participants (See section 3.2.1)
- analyse the impact on quality of life, via self-reported questionnaires throughout the study
- collect cancer samples (already collected as part of standard of care at diagnosis) and blood samples, to look for biomarkers which could help researchers explain or predict in which patients the treatment is most effective for and why.

By agreeing to participate in this study you will allow the collection of important data on your disease which could improve scientific knowledge about it and improve the ways to treat it. The research may also reduce the need for chemotherapy in some people as dostarlimab will be given as an alternative. The results of this research will not be added to your medical file and will of course remain anonymous.

1.6 Who is funding and organising this study?

This study is funded and sponsored (legally responsible for the study) by ARCAGY-GINECO (a French based group). This study is represented and coordinated in the United Kingdom by the Centre for Trials Research (CTR) located at Cardiff University.

2 WHAT DOES THIS STUDY INVOLVE?

This study will be carried out among 260 patients with advanced or metastatic womb/uterus cancer, in more than 80 healthcare facilities in 12 countries (United Kingdom, France, Belgium, Spain, Italy, Germany, Canada, Switzerland, Korea, Singapore, Australia and Turkey), for 8 years. Around 60 patients should participate in United Kingdom (across 12 NHS hospitals). Data concerning your health status and any subsequent treatments will be collected.

The study is divided into 5 stages:

1. the collection of a cancer sample (done standardly as part of normal clinical care at time of diagnosis, this is **not** an extra procedure).
2. Check participants meet the criteria for inclusion in the study. This is done by your doctor.
3. Random allocation to one of two treatment groups.
4. The treatment period.
5. The follow up period.

The duration of participation in this research study for each patient is around 5 years.

Stage 1-2

If you decide to take part in this study and provide your consent. Your cancer sample will be analysed by the laboratory at your hospital, to confirm an abnormality to the DNA repair system (named MMR deficient (or MSI High)). This is the type of cancer this study is investigating.

Once this has been confirmed a small part of the same cancer sample will be sent to a central laboratory in France (where the sponsors of this study are based) where a study pathologist will analyse the sample to confirm the result. If the sample confirms you are eligible and you wish to take part your doctor will explain more about the study including when, for how long and how to take the study treatment.

If the study pathologist does not confirm the abnormality is present, you will be informed, and unfortunately will not be eligible to participate in the DOMENICA study, and you will receive the standard of care treatment available within the NHS.

Stage 3

In order to find out if dostarlimab works as a treatment, it is necessary to compare this treatment (group 1) who will receive dostarlimab, to the standard treatment (group 2), which would be the treatment you would receive outside the study as part of standard of care within the NHS:

- Group 1 (study treatment): dostarlimab for 2 years maximum or until progression of your cancer

- Group 2 (standard treatment): chemotherapy called carboplatin and paclitaxel for around a maximum of 5 months

In order to be able to make comparisons, it is necessary that the distribution between the 2 groups is randomly selected by a computer: this is called **randomisation**. This ensures that the two groups are as similar as possible at the start of the study, so that the only thing that differs between the groups is the type of treatment received. This allows a fair comparison between the two groups. Neither you nor your doctor can choose a group or know, in advance, which group you will be allocated to as this may introduce differences between the groups. There will be the same number of patients in each group so you will have a 50:50 chance of being in Group 1 or Group 2. Your doctor will inform you of your group allocation once you have been randomised on the system.

Stage 4

The treatment period will be different for each group:

- Group 1 (study treatment): dostarlimab for 2 years maximum or until progression of your cancer

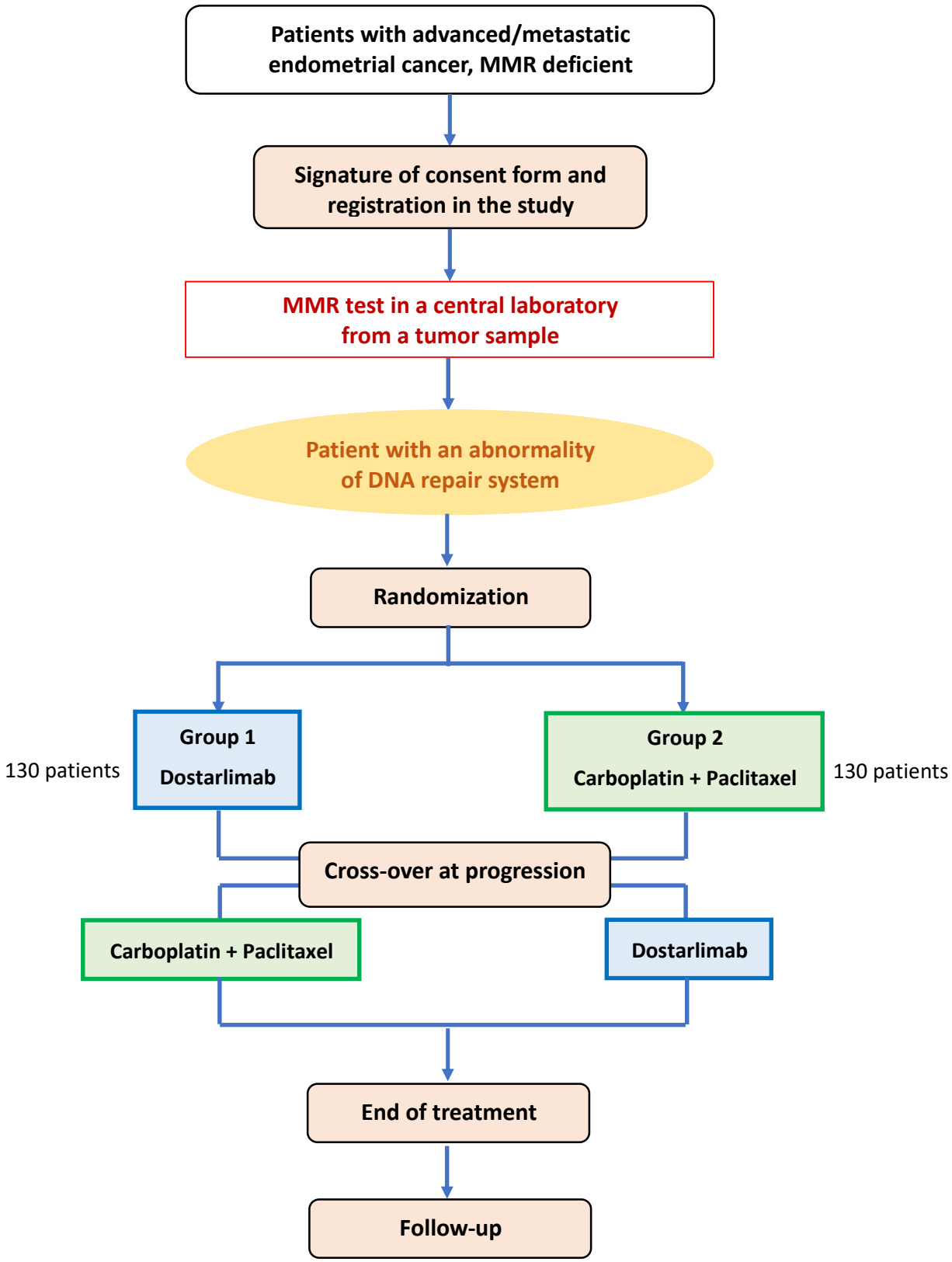
- Group 2 (standard treatment): chemotherapy called carboplatin and paclitaxel for around a maximum of 5 months

To optimise your chance of treatment, if your cancer progresses your doctor will evaluate your treatment and assess if you can change treatment group, this is called a cross-over.

Stage 5

The follow-up period is up to 2 years after you have completed your treatment.

FIGURE 1: DOMENICA STUDY DESIGN



2.1 Collection of cancer samples

When you decide to take part in this study and sign your consent form, you are agreeing for your cancer sample to be used during the study, this sample is already collected during a previous surgery or biopsy as part of standard routine care. This sample will be used to confirm the result of MMR test done locally at your hospital to check you have the type of cancer this study is investigating. If confirmed, your sample will be sent to a central laboratory in France for analysis by a DOMENICA study pathologist.

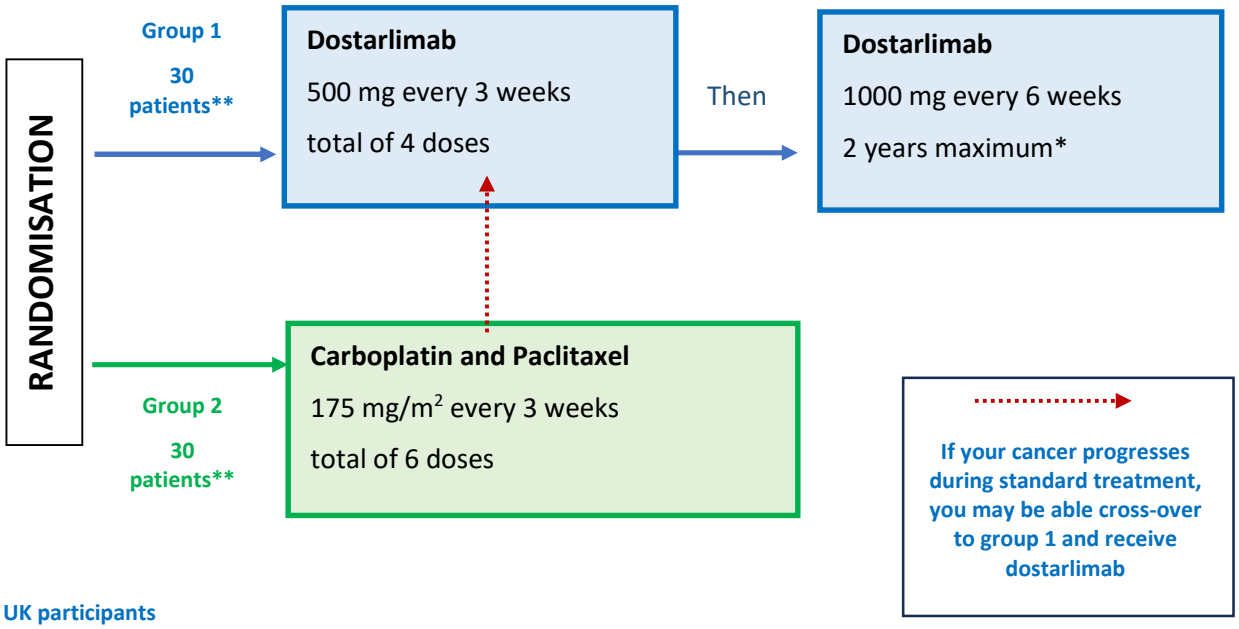
2.2 Your treatment

If you agree to take part in the study, your treatment will be randomised, and you will receive either:

- the study treatment (Dostarlimab) intravenously through an infusion (group 1): at a dose of 500 mg every 3 weeks for 3 months (a total of 4 doses), then at a dose of 1000 mg every 6 weeks for 2 years maximum (depending on your cancer status).

- Or the standard treatment (Chemotherapy: carboplatin and paclitaxel) intravenously through an infusion (group 2): chemotherapy- at a dose of 175mg/m^2, every 3 weeks for 5 months (a total of 6 doses).

FIGURE 2: TREATMENT DESIGN



** UK participants

If your disease progresses, if side effects become severe, or if new information indicates that this treatment is no longer suitable for you (whether it is the study treatment or the standard treatment), you will be informed by your doctor who will offer you other treatment options.

2.2.1 Can I move between treatment groups?

If your disease progresses (your cancer grows), and your doctor thinks you may benefit from a second treatment in the study you could receive it after Sponsor approval.

If you are in group 1 (dostarlimab) and your Doctor and Sponsor agree you will be allowed (should you wish) to cross-over to the chemotherapy arm (group 2).

If you are in group 2 (chemotherapy) and your Doctor and Sponsor agree you will be allowed (should you wish) to cross-over to the study treatment arm (group 1) and receive dostarlimab.

2.2.2 Do I have to avoid any medicines?

If you agree to take part in the study, and if your cancer has the mutations, known as MSI-high or dMMR, there are certain groups of medications that you will not be allowed to take while you are taking part in the study because of the way they interact with the study treatment. These medications include other approved or investigational anticancer treatments, investigational drugs, live vaccines, immunosuppressive agents and systemic corticosteroids.

You should inform your doctor of any medications that you are taking, and if necessary, they will try and find an alternative for you. If there is no alternative, you may not be able to take part in this research. You will not be asked to stop any medications that you need.

Some herbal and dietary supplements and some vaccinations may interact with the study treatment, so need to be discussed with your doctor before they are taken.

If you were to take any of these or if you are in doubt, contact your doctor.

2.3 Exams and visits schedule

If you agree to participate in this study, you will be expected to attend additional visits and have extra blood tests and scans beyond standard treatment, as outlined in section 2.3.5 to assess your health.

You will also be asked to regularly complete Quality-of-Life questionnaires and questionnaires on potential undesirable effects that could occur after the 1st dose of treatment:

- Four questionnaires to assess your quality of life (QLQ-C30, EORTC QLQ-CIP20, EORTC QLQ-EN24 and EUROQOL EQ-5D): about 80 questions in total;
- Approximately 60 questions to collect potential side effects.

Questionnaire completion will take about 35 minutes.

If you are over 70 years old, you will be asked to complete three additional questionnaires before the start of treatment (ADL, IADL and HADS): about 30 questions in total, requiring 10 minutes for completion.

2.3.1 Prior to treatment

Once you have given your consent to participate in this study (by signing three copies of the consent form), you will need to attend hospital where your doctor will ask you about the history of your cancer, past or current diseases, the treatments you have already received as well as any you are currently taking.

During this visit a medical examination will be carried out including:

- A complete physical examination (body weight, height, vital signs, ECOG performance status & gynecological examination),
- Blood test (a blood sample of about 30 ml / 3 tubes – approximately 6 teaspoons),
- An evaluation of your thyroid (a gland in your neck) function through a blood sample,
- Urine analysis,
- Electrocardiogram (ECG) to check your heart,
- A pregnancy test (if you are of childbearing age)
- Imaging (CT or MRI scan) of your cancer
- Ultrasound scan (to confirm hysterectomy or oophorectomy where operation notes are not visible)

If some of these evaluations have been done very recently, they will not need to be repeated.

If eligible, you will be asked to complete the required questionnaires on your quality of life and any potential undesirable effects, throughout the study, either on a computer or a tablet computer in clinic.

If you agree to participate in the research and sign the consent form for this, you agree:

- To give an additional blood sample for future exploratory research on the factors which could affect the treatment for this type of cancer. This blood sample (around 30 mL (i.e., 3 tubes) – approximately 6 teaspoons) will be collected at the initial clinic visit with the blood sample for biological/blood testing.
- To give a sample of your cancer (collected during a previous surgery as part of standard care) which will be sent to a central laboratory for biomarker analysis.
- To give an additional blood sample (if you are in group 1), for optional biological research to better understand treatment activity and the effect of antibodies on its presence in the blood.

Following providing informed consent and your doctor/study team confirming you are eligible to take part in the study you will be randomised to one of the 2 treatment arms (groups); the treatment will start within 7 days. Your doctor will inform you of your treatment group as soon as they know which group you are assigned too.

2.3.2 During the treatment phase

If you meet all the criteria to take part in the study your doctor will confirm the date you will start treatment and the frequency of visits required to monitor health according to the following schedule:

- **Group 1** (dostarlimab): you will have a visit with your doctor every 3 weeks (i.e. 4 visits), then, every 6 weeks until the end of treatment (for 2 years at maximum)
- **Group 2** (chemotherapy carboplatin and paclitaxel), you will have a visit with your doctor every 3 weeks (i.e. 6 visits)

If you change treatment group at progression of your disease (cross-over), the frequencies stated above will remain unchanged and all assessments detailed below will be performed.

Each visit will consist of:

- A complete physical examination,
- Blood testing (blood sample of about 20 mL (i.e., 4 tubes)),

- Urine testing,
- An evaluation of your thyroid (a gland in your neck) through a blood sample,
- Some questions on your health status since your last visit, and a collection of the treatments/medicines that you have taken and/or are currently taking.

Assessments by imaging (CT or MRI scan) to assess the cancer will be every 6 weeks for the first 26 weeks (approximately 6 months), every 9 weeks between weeks 26-52 (approximately 6 months) then every 12 weeks up to 2 years after starting treatment.

Some additional exams could be requested by your doctor to include:

- A blood clotting test
- A CA-125 dosage (marker of your disease). If there is anything unusual in the result of this dosage, an evaluation by CT or MRI scan could be requested by your doctor.
- An electrocardiogram (ECG) to check your heart.

NOTE – these additional exams could also be requested by your doctor at the end of the treatment phase.

You will also be required to complete (online or on the tablet computer in the clinic) a questionnaire on any undesirable side-effects you may experience (every 3 weeks until the 6th treatment dose, i.e., until week 18, then 6 weeks), and questionnaires on your quality of life (every 12 weeks).

Additional samples will also be requested, a full list of these is included within 2.4 Biological research.

2.3.3 At the end of the treatment phase

Regardless of your treatment group, you will have a consultation with your doctor within 30 days of treatment discontinuation and/or prior to switching treatment group (cross-over) if your disease progresses and sponsor approval is provided.

Usual medical examinations necessary for the monitoring of your health status will be carried out: a complete physical examination, an evaluation of possible side effects, blood testing (blood sample of about 30 mL, i.e. 4 tubes), some questions on your health status since your last visit and a collection of the treatments you have taken and/or are currently taking.

You should also complete (online or on the tablet computer in the clinic) a questionnaire on your potential undesirable effects that you may have experienced.

2.3.4 Follow-up after treatment

If your disease has not progressed but you have stopped your treatment for another reason, your doctor will request that you attend clinic every 6 weeks during the first 6 months, then every 9 weeks for the remainder of the 1st year, moving to every 3 months thereafter to monitor your health until progression. Your cancer will be monitored through regular scans.

If your disease progresses during the follow up phase, your doctor will evaluate if the cross-over to the other group of treatment would be a possible treatment option. If so, all assessments explained in the section 2.3.3 will be performed before starting the new treatment.

During these visits, the following examinations will be carried out: a physical examination, an evaluation of possible side-effects and questions to identify whether you are receiving any other anti-cancer treatment.

You should also complete (online or on the r tablet computer in the clinic) the questionnaires on your quality of life every 12 weeks and a questionnaire on your potential side-effects every 6 weeks.

2.3.5 General overview of planned visits during the study

Procedures	Visits			
	Maximum 28 days before treatment	**Phase of treatment**	**End of treatment (Within 30 days after last dispensation or before cross-over)**	**Follow-up after treatment**
Informed Consent Signature	X			
MMR/MSI Status, local and central testing	X			
Medical History	X	X		
Physical examination	X	Before each dispensation of treatment	X	X
Cancer assessments by Imaging (CT or MRI scan)	X	Every 6 weeks during 6 months, then every 9 weeks until the 1st year of treatment, then every 12 weeks		
Electrocardiogram (ECG)	X	At investigator's discretion		
Pregnancy test (serum or urine) – if applicable (see 3.2.3.1)	X	Prior to each cycle during the entire treatment period	X	X
Biological testing + urine test + CA-125 test + thyroid test	X	<u>Group 1:</u> Every 3 weeks until week 9 Then every 6 weeks <u>Group 2</u> every 3 weeks	X	
Pregnancy test (if applicable)	X	Before each dispensation of treatment		
Questionnaires on Quality of Life to be completed through a tablet computer.		Every 12 weeks		
Questionnaire on undesirable side-effects to be completed through tablet computer		Every 3 weeks until the 6th treatment dose, i.e., until i.e.; week 18, then 6 weeks		
Blood sample for biomarker analysis (1) (mandatory)	X	Before the 2nd and 5th course of treatment		
Cancer sample for biomarker analysis (1) (mandatory)	X			
PK and IG when treated with dostarlimab (group 1)		Before treatment at cycles 1, 2, 4, 5, 9 (PK and IG) and PK only after the treatment at Cycle 1	End of treatment visit only	12 weeks after end of dostarlimab
Dispensation of dostarlimab (group 1)		*Every 3 weeks during 3 months, then every 6 weeks for a maximum of 2 years*		
Dispensation of chemotherapy per Paclitaxel and carboplatin (group 2)		*Every 3 weeks for 4 months*		

(1) In case of progression, and if you agree, a blood sample about 30mL (i.e.,3 tubes) and a cancer sample will be stored for future Research

2.4 Biological Research

In addition to the main DOMENICA study there is also a biological sample collection aspect to the study called translational research, often performed by scientists in a laboratory. The purpose of this translational research is to help us understand why different people may react differently to medicines.

Biomarkers are molecules (for example, proteins, lipids or genes) found in our blood or tissues. Different biomarkers may affect how a disease progresses or not, as well as how a body reacts to drugs like those provided in this study. The sponsor of this study, ARCAGY-GINECO, would like to determine if there is a link between the presence of biomarkers in the cancer sample cells and the effectiveness and side effects of the study treatment. The goal of this research is to determine if some individual biomarkers or cancer-based characteristics would allow, in the future, to identify the patients who benefit most from this new treatment.

If you decide to participate in the main study, then you will also be approached to participate in the translational research requiring:

- 2 samples of your cancer, which have been taken during a previous surgery before your inclusion in the study, in addition to the cancer sample needed for the confirmation of MMR status.
- A blood sample about 30 mL (i.e.,3 tubes) before the study treatment
- A blood sample about 30 mL (i.e.,3 tubes), during your visit for the second cycle of your treatment
- A blood sample about 30 mL (i.e.,3 tubes), during your visit for the fifth cycle of your treatment

In case of progression, and if you agree, a blood sample about 30mL (i.e.,3 tubes) and a tumour sample (taken under imaging) will be stored for Translational Research. **This is optional**.

The genetic characteristics of your cancer will be analysed. It will be necessary to compare these characteristics to those of your DNA (your genetic characteristics located in all the cells of your body). The blood sample taken before treatment will be used as a comparator.

These analyses will not be carried out in order to study your own genetic characteristics, nor to identify you, but in order to better understand the mechanisms of your disease and its treatment.

2.5 Biological research – Dostarlimab group only

If you are randomised to group 1, Dostarlimab you will be asked to take part in additional optional biological research. This research will involve taking additional blood samples during your treatment stage. These blood samples will be analysed for Pharmacokinetics (also known as PK) which measure the dostarlimab rate in your blood along with Immunogenicity (also known as IG) which define the specific antibodies that can bind to dostarlimab during treatment. The purpose of this optional research is to better understand the study treatment activity and the effect of the antibodies. dostarlimab. Extra blood samples will be collected at different time points including:

- Blood sample of 2mL and 4 mL will be drawn before administration of study treatment at Cycles 1, 2, 4, 5, 9; at end of treatment visit and then 12 weeks after
- Blood sample of 2mL after administration of study treatment at Cycle 1

3 WHAT ARE THE POTENTIAL BENEFITS & RISKS OF TAKING PART?

3.1 What are the benefits of taking part?

We hope that dostarlimab is effective at significantly reducing the rate of relapse of advanced or metastatic womb/uterus cancer.

If successful this study could potentially help patients get quicker access to the study drug, dostarlimab.

If you participate in this study, you will have access to immunotherapy much sooner than you otherwise would. However, you may not benefit from participating in this study. Your condition may remain the same, improve or worsen. Your participation will not limit the access to the standard treatments, in case of benefit or progression after the treatments dispensed in this study.

By participating in this research, you will be helping scientists and clinicians better understand the disease and improve future treatment options. The information from this study will also hopefully help future womb/uterus cancer patients.

3.2 What are the potential risks and disadvantages of taking part?

Study treatment may be responsible for some side effects. All of them are not identified, even though drugs proposed in this study have all been marketed in many countries worldwide for several years. Most of them are variable from one patient to another. They can be mild, moderate, or sometimes severe. Some may go away as soon as you stop taking the study treatment. In some cases, they can be serious, long-lasting or may never resolve (irreversible). If you experience any side effects, your doctor will give you medicines to help reduce the side effects where possible.

It is important that you inform your doctor of any medication, dietary supplement, herbal supplements, that you are taking or intend to take during the study as interactions may exist between the drugs.

The safety of study treatment will be assessed at each visit by your doctor. Additional treatments may be prescribed to control side effects. If they are significant, your doctor may change the treatment doses or stop study treatment for a given time or permanently. Likewise, it is important that, apart from these regular visits, you contact your doctor immediately in the event of uncomfortable toxicity.

The following sides effects may occur based on the experience from other patients who have been treated with dostarlimab. They are listed according to their frequency regardless of their severity.

If you experience any of the side effects listed below, please contact your doctor immediately.

3.2.1 Dostarlimab side effects

Very common (> 10 %)

- ***Anaemia****: Decreased number of red blood cells (which can lead to fatigue or breathing difficulties and require a blood transfusion)*

- ***Increase of transaminases*** *(AST, ALT which are produced by the liver)*

- ***Gastro-intestinal disorders:*** *Nausea, diarrhoea, vomiting*

- ***Cutaneous reactions:*** *Skin rash (*pimples, patches or redness*), pruritis (itching)*

- ***Fever***

- **Hypothyroidism:** Insufficient secretion of hormones by the thyroid, which could cause especially fatigue, hypothermia, and weight gain

Common (1-10 %)

- **Adrenal insufficiency**: Insufficiency of secretion of steroid hormones by adrenal, which could lead to important fatigue, a decrease of blood pressure and weight loss

- **Hyperthyroidism:** Over-secretion of hormones by the thyroid, which could cause weight loss, diarrhoea, nausea, heart palpitations, and insomnia

- **Pneumonia:** An infection that irritates the lungs

- **Pancreatitis:** Pain in the upper abdomen. This could become severe and cause nausea and vomiting, fever, and rapid heart rate.

- **Gastro-intestinal disorders:** Colitis (Inflammation of your digestive track)

- **Flu like syndrome** with fever, myalgia (muscular pains), chills

Uncommon (0,1-1%)

- ***Auto immune haemolytic anaemia****: Dysfunction of the immune system which produces auto antibodies that attack the blood cells as if they were substances foreign to the human body, which could cause fatigue and shortness of breath*

- ***Inflammation of thyroid gland*** *(thyroiditis), which can result in a malfunction of the thyroid gland (resulting in hypo or hyperthyroidism)*

- ***Inflammation of pituitary gland,*** *located in the brain (Hypophysitis) which could cause pale appearance, hair loss, and slow speech*

- ***Diabetic ketoacidosis****: Increase of blood acidity, related to the accumulation of toxic substances caused by the lack of insulin*

- ***Type 1 diabetes:*** *Excess of blood sugar that can lead to abnormal thirst, and fatigue*

- ***Immune-mediated arthritis****: Inflammatory articular disease characterised by articular pains*

- ***Muscular rheumatism*** *(Polymyalgia rheumatica)*

- ***Nephritis:*** *Inflammation of kidneys, which could cause some disorders of substances by the kidney*

- ***Uveitis:*** *Inflammation of eye*

- ***Myasthenia:*** *Disease which can lead to fatigue and muscle weakness*

- ***Infection in the brain*** (encephalitis)

- ***Inflammation of the heart muscle*** *(myocarditis)*

- ***Inflammation of the liver*** *(hepatitis)*

- ***Inflammation of the lining of the stomach*** *(Gastritis)*

- ***Inflammation of the food pipe*** *(Esophagitis)*

- ***Inflammation of the small intestine*** *(Enteritis)*

- ***Inflammation of blood vessels in the gastrointestinal tract*** *(Vasculitis gastrointestinal)*

- ***Inflammation of the muscle*** which can cause weakness, swelling and pain *(Myositis)*

- ***Inflammation throughout the whole body*** *leading to high or low temperatures, low blood pressure, increased heart rate, increased rate of breathing and low or high white blood cell count (Systemic Inflammatory Response Syndrome)*

- ***Infusion-related reactions*** *which can occur within 24 hours after receiving an intravenous infusion, or which can be delayed for up to about 2 weeks. Infusion-related reactions may include dizziness or fainting, flushing, rash, fever, chills, shortness of breath, increased or decreased blood pressure, increased heart rate, swelling of the lips, tongue, or face, feeling sick to your stomach, back pain or pain at the site of infusion. Although infusion-related reactions are usually reversible, they can be severe or life threatening. (Infusion related reactions)*

Rare but serious immune-related adverse events seen when dostarlimab was used alone or in combination with other medicines:

- Overactive immune-system cells which damage body tissues and organs leading to signs of uncontrolled fever, enlarged spleen, low blood count and liver test abnormalities.

- A neurological disorder where the immune system attacks part of the peripheral nervous system that can cause tingling in the feet and hands, pain, muscle weakness, and problems with coordination (Guillain-Barre syndrome).

There may be other risks called class effects that have been seen in patients receiving other drugs that work like dostarlimab. These effects could also occur with dostarlimab. They are potential risks but not known as side effects for dostarlimab so far. The most significant class related side effects are "immune-related", meaning side effects caused by increased activity of the immune system, which can affect multiple organs of the body including gastrointestinal tract, endocrine system, cardiovascular system, lungs, liver, skin, musculoskeletal system and nervous system.

The side effects listed below require immediate medical attention or advice.

Call the study doctor right away if you have any of these side effects.

- Respiratory: Shortness of breath, rapid breathing, new or worse cough
- Gastrointestinal: Diarrhoea, stools that are black or bloody, stomach area pain, nausea or vomiting
- Kidneys: Dark or bloody urine, urinating more often than usual
- Musculoskeletal: Chest pain, muscle pain or weakness
- Cardiac: Fast or unusual heartbeat
- Skin: Rash, itching, blisters, pale or yellow skin
- Eyes: Yellowing of the whites of your eyes, blurry vision
- Brain: Abnormal thinking, confusion, personality changes, headache, and neck stiffness
- General: Bleeding or bruising more easily than normal, feeling cold, hair loss, dizziness or fainting, feeling tired or weak, fever or chills.

3.2.2 Chemotherapy side effects

Chemotherapy (carboplatin or paclitaxel) can cause specific side effects. Your doctor will explain these side effects.

3.2.3 Risks linked to study procedures.

If you take part in this study, you may have a ***CT**** brain scan, ***CT**** chest abdomen and pelvis scans and potentially ***CT**** guidance for a cancer biopsy. ***CT**** and ***MRI**** scans may involve an injection of a ***contrast agent****. As with any product, there is a risk of an allergic reaction to that product.

CT* **scans** - Some or all of these procedures 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 and provide your doctor with other clinical information. Ionising radiation may cause cancer many years or decades after the exposure. In patients with your current clinical condition, the chance of this happening to you is extremely small.

Scans may involve an injection of a contrast agent. As with any product, there is a risk of an allergic reaction to that product. Needle pricking during injection of the contrast agent can cause pain, swelling, bruise, irritation, or redness.

MRI scans - These procedures use non-ionising radiation to form images of your body and provide your Doctor with clinical information to make informed decision. Some (around 2) of these procedures will be extra to those that you would have if you did not take part.

During the electrocardiogram (ECG), you may experience itching or bruising on the skin where the patches were placed.

Needle pricking during injection of the treatment administration or blood sampling can cause pain, swelling, bruise, irritation, or redness.

3.2.3.1 Pregnancy and breastfeeding

As the sponsor of this research does not know the effects of the study treatment on an unborn child or newborn, you are not allowed to participate in this research if you are pregnant or if you plan to become pregnant during the study period.

People of childbearing potential can only participate in this research if they use effective contraceptive methods. You will be required to use one highly effective form of contraception with your partner starting from the Screening Visit through 120 days after the last dose of study treatment.

You will need to perform a pregnancy test before starting the study and regularly during the study if your doctor deems it necessary. The pregnancy can be reliably detected through the pregnancy test just a few days after the conception.

Breastfeeding women cannot participate in this research because the treatment may pass into the child's body during breastfeeding and the problems it may cause the child is not known. Therefore, breastfeeding is not allowed during treatment and for up to 120 days after the last dose of the study treatment.

During the study and up to 6 months after the last dose of study treatment, **please inform your doctor immediately if pregnancy occurs or is suspected.** Your study treatment will be stopped immediately.

If you and your partner agree, the sponsor will ask you for information on the outcome of your pregnancy (such as your health, the date of conception, the progress of your pregnancy, the treatments that you could receive and at the birth of the child, information about its health).

4 WHAT ARE MY RIGHTS AND THE LEGAL PROVISION FOR THIS STUDY ?

Medical research is strictly regulated by law. The legal provisions guarantee a number of rights.

Please read this section carefully.

4.1 Conditions for participation

Your participation in the study is free and voluntary. If you agree to take part in this study, you will need to sign a consent form to participate.

You cannot have participated in any other interventional study in the 3 months preceding the start of your participation to DOMENICA study, and you will not be allowed to participate in any other study at the same time as you take part in the DOMENICA study.

4.2 Commitment from your side

During your involvement in the study, you will be required to follow the instructions given by your doctor. It is important to come to the hospital for every planned visit to receive treatment, perform the examinations, including scans, and be assessed by your doctor. It is important that you inform your doctor of any change in your state of health, even if it is not related to the study treatment and/or any change in medication intake.

4.3 Right to withdrawal

You are still free to withdraw your consent at any time without giving any reason and stop taking part in the study. Your decision will not affect your medical care now or in the future. To ensure and preserve your safety, we ask you to inform your doctor immediately about your decision. In this case your doctor will discuss with you your alternative treatment options.

In the event of withdrawal, your personal data and the blood or tumour samples already collected may be analyzed unless you express your refusal.

4.4 Alternative treatments

Your doctor will discuss with you the supportive care options and the risks and benefits associated with all of them.

4.5 What happens if I am injured while I am in the study?

Injuries that have been caused by the study medication, tests or procedures are called 'research injuries'. Injuries caused by your usual medical care or your cancer, are not research injuries.

In the event that something goes wrong and you are harmed during the research study, there are no special compensation arrangements beyond your rights as an NHS patient.

If you are harmed and this is as a result of the study medication, tests or procedures 'research injuries' then you may have grounds for legal action for compensation against the Sponsor (ARCAGY-GINECO), but you may have to pay your legal costs. If you are injured due to someone's negligence the normal National Health Service complaints mechanisms will be available to you; your study team at your hospital site are covered by NHS Indemnity.

If you have private medical insurance, you should tell your insurer that you are taking part in research. They will let you know if it affects your policy.

4.6 Compensation

You will not receive any compensation for taking part in the study. You will not have to spend any money to participate in the study. The study treatment will be given to you free of charge and you will not be charged for study consultations nor examinations.

There is potential you will have to attend up to two additional visits outside standard care. Any travel costs associated with these visits will be reimbursed by the trial team. Your trial team will discuss reimbursement for reasonable travel costs with you and organise reimbursement. You should submit claims as described by your trial team within 3 months of each visit.

4.7 Approval from Competent Authorities

In accordance with relevant regulation, the DOMENICA study has received a positive outcome and approval by the responsible Ethics Committee and has also been approved by the responsible regulatory authorities within each of the countries in which the trial will be conducted.

4.8 Right to confidentiality

Information that can identify you will never be revealed. To carry out this research, your doctor will send data from your medical file to ARCAGY-GINECO. Transmission and data communication will be done under the rules of professional secrecy.

Representatives from ARCAGY-GINECO will not be able to see your hospital or clinic records. This access can only be carried out under the responsibility of your doctor.

In addition, in case of an inspection mandated by the competent regulatory authorities, the inspectors in charge of this mission of public interest may be required to consult your personal data collected as part of the study and thus have direct access to your medical files.

All persons having access to these medical and personal data are required not to disclose or reveal such information. They are subject to the conditions of professional secrecy.

4.9 Storage and use of biological samples

Blood and cancer samples collected as part of the DOMENICA study will be stored at the hospital site where you are being treated. They will be stored there under appropriate conditions and in accordance with the current regulation until they are transferred at the central laboratory of the Curie Institute - Hôpital Claudius Régaud, 26 rue d'Ulm, 75005 Paris, France for storage. Subsequently, they will be transferred to ARCAGY-GINECO's partner laboratories for analysis. These laboratories may be located inside or outside the European Union.

Your samples will be analysed during or at the end of the study, therefore this could be several months or years after signing your consent. If any of your blood or cancer samples have not been fully used for the analysis performed at the end of the study they will be destroyed unless you have provided consent for the optional translational element of the trial then they will be stored, and additional scientific research on womb/uterus cancer may be carried out by ARCAGY-GINECO until all your biological material is used.

All current and future analysis performed on these samples will be carried out for research purposes only. Your samples will be handled and stored according to current laws. Your samples will be labelled with a unique number, and without any personal identifiable information such as your name or date of birth. To guarantee the confidentiality of information, data concerning the collection of blood and tumour samples will be kept in a secure database.

Your samples may be stored by ARCAGY-GINECO after the end of the DOMENICA study without a time limit and until all biological material is used.

The results of tests on your biological samples will be compared and combined with those of other studies on the treatment under evaluation. In addition, they can be compared to medical information collected about you during the study, but only if this information can help us to better understand how patients respond to the study treatment. The results of these tests will have no influence on the medical management of your cancer.

At any time, you can withdraw your consent to the future use of your samples by communicating your request to your doctor who will send such request to ARCAGY-GINECO who will ensure that any remaining samples are destroyed. Your request will be recorded in your medical file. This will not affect the medical care you will receive, or the data already generated with your samples.

Furthermore, if you withdraw your consent to participate in the research, samples already collected may still be used, unless you expressly request that they be destroyed or if local laws require their destruction. However, any results generated before you stopped participating may be kept by ARCAGY-GINECO.

4.10 Right to information

If you have any questions about this study, please ask your doctor who will provide you with all the information you would need on the study drug or your participation.

Throughout the course of the study, you will have the right to be informed on this research. Your doctor will also provide you with all new information that may modify your decision.

4.11 Communication of results

Your participation in this study allows improvement in biological and medical knowledge. According to the provision of law n°2002-303 of March 4, 2002, relating to the rights of patient, you are allowed to know the overall results of this study by making a request to your doctor. The design of the protocol and its results will be published and available in at least one public website (http://www.arcagy.org).

The study results will be published in a scientific journal. They will also be presented at international scientific conferences. These results will be strictly anonymous; it will be impossible to identify you. It may take a long time for the first results to be presented (between 2 to 7 years after the start of your participation).

At the end of DOMENICA, a lay summary of the results of this study will be sent to the doctors at the participating hospitals and they will be asked to explain the results to the patients involved.

5 CONFIDENTIALTY AND PROTECTION OF PERSONAL DATA

5.1 How will we use information about you?

We will need to use information from you and your medical records for this research project.

This information will include:

- Initials
- Your full name
- NHS number
- Date of birth
- Clinical information relevant to your care

Your doctors and nurses will use this information to do the research or to check your records to make sure that the research is being done properly.

ARCAGY-GINECO is the sponsor for this study and is based in France. ARCAGY-GINECO will be using information about you in order to carry out this study and will act as the data controller. The data controller is responsible for making sure your information is used properly.

People, such as staff from the Centre for Trials Research (CTR) at Cardiff University, who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. All your information will be sent to France who will follow our rules about keeping your information safe.

Once we have finished the study, the Sponsor ARCAGY-GINECO will keep some of the data so they can check the results. They will write our reports in a way that no-one can work out that you took part in the study.

Some medical data could also be shared anonymously with the pharmaceutical company which produces dostarlimab. This is only for tolerance/safety purposes and, in accordance with the regulations, it will allow this company to have all information for the monitoring of this drug.

5.2 What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. Your samples/data will be stored at central laboratory of the Curie Institute -Hôpital Claudius Régaud, 26 rue d'Ulm, 75005 Paris, France.

5.3 Where can you find out more about how your information is used?

You can find out more about how we use your information at:

- www.hra.nhs.uk/information-about-patients/
- HRA patient leaflet available from www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to dpo@arcagy.org

5.4 What about confidentiality?

We will follow ethical and legal practice in accordance with the General Data Protection Regulation (GDPR). In the UK we follow the GDPR rules and have a law called the Data Protection Act. These laws mean that all information about you will be handled in confidence.

If you wish to make a complaint on how we have handled your personal data, you should contact the Data Protection Officer of your study hospital via your Research doctor or Nurse. This person will investigate further the issue by contacting ARCAGY-GINECO. Or you can contact the Data Protection Officer of ARCAGY-GINECO (dpo@arcagy.org). However, ARCAGY-GINECO may not be able to reply in your language. If you are not satisfied or believe ARCAGY-GINECO is using your personal data in a way that is not lawful, you can complain to the Data protection authority in your country.

5.5 How long will we keep your data?

ARCAGY-GINECO will keep coded information about you for at least 25 years after the study has ended. Every 5 years thereafter, ARCAGY-GINECO will assess whether it will or can keep your data. This assessment will take into account applicable legislation, the relevance of your data for scientific research, the scope of your consent and the choices you made.

[To be printed on local hospital headed paper]

DOMENICA study

Randomized phase III trial in MMR deficient endometrial cancer patients comparing chemotherapy alone versus Dostarlimab in first line advanced/metastatic setting.

DOMENICA CONSENT FORM

Centre Number:
Study Number:
Participant Identification Number for DOMENICA:

If you would like to take part in this trial, please complete this consent form by **initialing** the boxes and signing below. **Boxes 1-12 must be initialed for consent to be valid.**

1. I confirm that I have read the information sheet dated..... (version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I freely agree to take part in the DOMENICA study.	☐
3. I understand how my personal data and my biological samples will be collected, stored, and analysed.	☐
4. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. Your personal data and the blood or tumour samples already collected may still be used unless you express your refusal.	☐
5. I freely accept that blood and tumour samples will be collected and used for biological research purposes (including constitutional DNA analysis) by ARCAGY-GINECO in France. I understand that my samples will be anonymised, and I will not receive any feedback regarding the results. *If I do not initial in the box, I will not be able to participate in the DOMENICA study*	☐
6. I understand that the investigator may interrupt my participation in the research at any time if he/she deems it necessary.	☐
7. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from ARCAGY-GINECO, The Centre for Trials Research (CTR) at Cardiff University, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data.	☐
8. I understand that the information collected about me will be used to support other research in the future, and may be shared anonymously with other researchers.	☐
9. I agree to my General Practitioner being informed of my participation in the study / I agree to my General Practitioner being involved in the study, including any necessary exchange of information about me between my GP and the research team.	☐

10.	I am aware that this study has been approved by the relevant regulatory authority and Research Ethics Committee. The sponsor has taken out relevant insurance to cover any protocol related risks.	☐
11.	The overall results of the research will be provided to me at the end of the research, if I request it from my Doctor and I agree any data collected may be published in anonymous form in academic books, reports, or journals.	☐
12.	Three original copies of this consent form have been prepared: one has been given to me, the second has been kept by the study Doctor and will be kept in the study file for at least 25 years after the end of the research and the third will be kept within my hospital notes/record.	☐

<u>Optional Consent</u>: Not agreeing to the below points will have no impact on your participation this research:

13.	In case of my disease progressing, I freely accept that blood and tumour samples will be collected and used for Translational Research by researchers in France and other countries. I understand the research may involve DNA analysis, animal research or use by the commercial sector. The researchers will not be able to identify me from my sample.	YES ☐ NO ☐
14.	I freely agree that my coded personal data and biological samples may be used for further research exclusively for scientific purposes by researchers in other Universities or commercial companies in the field of cancer, including genetic research, and I understand that I can withdraw my consent at any time. Such research will include researchers who work outside of the United Kingdom. The research projects will be available on the sponsor's website http://www.arcagy.org	YES ☐ NO ☐
15.	If randomised to the Dostarlimab arm of the study I agree that additional blood samples can be collected before administration of treatment at cycles 1, 2, 4, 5, 9, at the end of cycle 1, at the end of the study treatment and 12 weeks after.	YES ☐ NO ☐

***When you have initialed all relevant boxes above, please complete the first box below. (Including the date) yourself*:**

.....	.....	.....
Name of Participant	Date	Signature
.....	.....	.....
Name of Principal Investigator	Date	Signature
.....	.....	.....
Name of Person taking consent (If different to Principal Investigator)	Date	Signature