Title of the study:

Study of Metastasis-directed Therapy for Oligoprogressive Castration-Refractory Prostate Cancer.

Official title: Metastasis-directed therapy in oligoprogressive castration-refractory prostate cancer: a randomized phase 3 trial

EU Number: 2022-502254-13-00

Study Number: S67130

Sponsor: University Hospitals Leuven (UZ Leuven)

Who can I contact if I have questions?

Principal Investigator:

Prof. dr. De Meerleer Gert
UZ Leuven, Department of Radiation Oncology, Herestraat 49,
3000 Leuven (tel: 016 34 69 02)

Study staff:

Dr. Rans Kato
UZ Leuven, Department of Radiation Oncology, Herestraat 49,
3000 Leuven (tel: 016 34 01 10). Contact for emergencies: 0476/85.61.39

Ombudsperson/patient rights: if you have any concerns about your rights as a participant: 016 34 48 18

The client's insurance company and the insurer's contact person: in the event of a dispute or complaint about a claim
Amlin Insurance SE, Van Breda Risk & Benefits NV, Plantin en Moretuslei 297, 2140 Antwerp.
Policy number: 299.053.700
Phone: +32 3 217 67 67
E-mail: info@vanbreda.be

Data Protection Officer of the Study Centre: if you have any questions about the confidentiality of your data. Email: dpo@uzleuven.be

Belgian Data Protection Authority: in case of complaints about the confidentiality of your data. Email: contact@apd-gba.be

THE STUDY AT A GLANCE

Dear patient,

You have been diagnosed with new and/or growing lesions on recent imaging that are metastases of the tumor in the prostate or a recurrence of the tumor in the region of the prostate (called local recurrence). These lesions are no longer sensitive to your current therapy, while the rest of the disease still responds to this therapy.

Therefore, we invite you to participate in a clinical trial (hereinafter referred to as a "study") that is intended to find out whether we can extend the patient's lifespan through metastasis-directed therapy.

Before you agree to participate in this study, we would like to fully inform you about what the study entails in terms of organization, the possible risks and benefits. This way you can decide for yourself about your participation. This is called **giving "informed consent".**

This chapter will already give you **an idea of** what this study entails. Nevertheless, we would like to ask you to read all the pages, even though it will take you a lot of time. It is important that you read and understand everything. If you don't do this, you will participate in the study without knowing what you're getting into. Therefore, please ask me all your questions.

In this study, two treatment strategies will be compared. The choice for one of the two treatment strategies will be made by lottery. You have 1 in 2 chance of being in group A: treatment without metastasis-directed therapy (active follow-up or treatment with next-line systemic therapy) and 1 in 2 chance of ending up in group B: metastasis-directed therapy by means of surgery or targeted radiation treatment while your current treatment with systemic therapy is continued. The duration of your treatment and your side effects depend on the locations of the metastasis(s) and will be discussed with you by your treating physician.

I can't tell you yet how long this study will take. Since we want to see in the study whether we can extend the life of the patient, you will be monitored for as long as you live. However, this follow-up is according to the standard follow-up schedule in patients with metastatic prostate cancer. You will also have to fill out questionnaires at some times.

It is particularly important that you know that all treatments can have **side effects**. Therefore, you must understand that you **must report these side effects or any new health problem to me.**

The sponsor, UZ Leuven, has taken out insurance for this study .

During the entire period of this study, it is **not allowed to get someone pregnant.** The use of a good method of contraception is necessary and will be discussed with you.

The **treatments and examinations that are study-specific** will be paid for by the sponsor and **will not be charged to you**. The treatments and examinations that are part of your standard treatment will be charged to you or your health insurance fund (Belgian social security).

The data collected during this study will be treated confidentially.

One thing I would like to emphasise very strongly is that you are absolutely not obliged to participate in this study. Even if you have started your studies, you can always leave. I will always fully understand that and continue to take care of you as before.

The study was evaluated by the government and an ethics committee. Just because they have approved this study doesn't mean you should feel obligated to participate.

In order to participate in this study, you must, for your own safety, agree that I, as an investigator, will inform your treating physicians of your participation in this study. You may not participate in another clinical trial at the same time without informing the investigator or study staff. We may refuse to participate for reasons for reasons. It is also important that you cooperate and follow the instructions that the study staff and I give you regarding the study. You will be given an "emergency" card, which states that you are participating in a clinical trial. You must have this card with you at all times; This is necessary for your safety should you need emergency treatment in a hospital where you are not known.

If you agree to participate, please sign the informed consent form. I will also sign the form and thereby confirm that you have received the necessary information about the study. You will receive a signed and dated copy of the form.

Now that you already have some idea of what this study entails, you can read the other pages of this document. You don't have to do that all at once. Above all, it is important that you understand what you are reading. If you wish, you can also discuss this study with other confidential advisors (such as your doctor, family or friends). My staff and I are also ready to help you if there are things that are not clear. It's our job to make sure you understand everything well.

Best regards,

Your treating physician and researcher,

Prof. Dr. De Meerleer Gert
Dr. Rans Kato

CHAPTER I – DESCRIPTION OF THE STUDY PROGRAMME AND YOUR RIGHTS TO PARTICIPATE

1. Why are we doing this study?

When prostate cancer causes metastases, hormone therapy is traditionally started by performing surgical castration or hormonal injections. To this may be added other therapies such as chemotherapy, second-line hormone therapy, Radium-223. This can be done both at the start of treatment and in the further course of treatment when the disease progresses. However, if the progression of the disease is limited to a few lesions (maximum 5) and/or local recurrence, targeted treatment of these lesions can ensure that the disease remains under control for a longer period of time and it is hoped that the lifespan will be extended and that there is a possible improvement in the quality of life. From previous studies, this seems possible with minimal side effects. However, these studies require confirmation from a larger study, which is what we want to achieve with this research.

This study is a randomized, open trial in which two groups will be compared. We therefore want to investigate whether we can extend the patient's lifespan by means of targeted radiation and/or surgery on the growing or new lesions compared to a wait-and-see policy or the start of next line of systemic therapy. In addition, the side effects you experience, the quality of life and the cost-effectiveness of this metastasis-directed treatment will also be evaluated during the course of the study.

2. Why am I being asked to participate?

You have been diagnosed with new/growing lesions on recent imaging, which are metastases of the tumor of the prostate. These lesions are no longer sensitive to your current therapy, while the rest of the disease still responds to this therapy. Your treating physician has told you about the treatment options and the above-mentioned clinical study.

It is not certain that your participation in this study will cure your disease, improve your quality of life or prolong your life.

The investigator or study staff will discuss with you the conditions to be admitted to the study.

3. Do I have to participate in a study?

Your participation in a study is voluntary and should never be done under pressure. This means that you have the right not to participate in the study. You may also withdraw at any time without having to give a reason, even if you have previously agreed to participate. Your decision will not affect your relationship with the investigator or your treating physician, nor will it affect the quality of your future medical care.

If other treatments are available for your prostate cancer, you will discuss these treatments with you with the investigator or his/her representative.

If you do not wish to participate in the study, your treating physician will decide together with you which therapy will be administered. This can be the start of the next line of systemic therapy, a radiation treatment for the new or growing lesions or a wait-and-see policy. The treatment options will always be discussed at the multidisciplinary consultation. The investigator will discuss these treatments with you.

4. What will happen during the study?

This study will take place at the Department of Radiation Oncology of UZ Leuven. A total of 246 patients will be enrolled in this study. The sponsor of this study is UZ Leuven.

If you agree to this study, you will be randomized after signing this consent form. This means that the choice for one of the two treatment strategies is made by lottery. You have 1 in 2 chance of being in group A: treatment without metastasis-directed therapy (active follow-up or treatment with next-line systemic therapy) and 1 in 2 chance of ending up in group B: metastasis-directed therapy by means of surgery or stereotactic body radiation therapy while your current treatment with systemic therapy is continued. The classification into group A or group B is done in a random manner and cannot be influenced in any way by the investigator or patient. This is a frequently used method of research when one wants to compare treatments objectively. The duration of your treatment and your side effects depend on the locations of the metastasis(s) and will be discussed with you by your treating physician.

If a metastasis-directed therapy is to be administered, your doctor will discuss with you whether this will be done by means of surgery or by very targeted radiation treatment. The targeted radiation treatment will be administered in single fractions. To choose between radiation treatment or surgery, we use the following general rules:

- Radiation treatment will be preferred over surgical treatment if it involves a metastasis in the bone, glands in the mediastinum (the space between the lungs), local relapse in the prostate region to previous surgery of the prostate.
- Surgery will be discussed with the patient in case of a recurrence in the region of the prostate after previous radiation treatment of the prostate, glands in the small pelvis or along the large blood vessels in the abdomen, glands in the neck, metastases in the lungs or liver (rare <10%), metastases in the adrenal gland (very rare) and brain metastases (very rare). If surgical treatment is chosen, it is assumed that a complete removal of the metastasis is possible.
- If both surgery and radiotherapy are a good option for the treatment of the metastasis, the patient's choice will be taken into account.

Each patient will be regularly monitored by the radiation oncologist, urologist and/or general medical oncologist. These checks will also take place if you would not participate in the study. So you will not undergo any additional checks in this study. Furthermore, you will be asked to fill in questionnaires at regular intervals during the follow-up that gauge your physical and emotional health, this takes about 10 minutes. These questions gauge complaints such as fatigue, pain,... The investigators will use this information to assess the impact of the treatment on your quality of life. If you don't feel comfortable filling in certain questions, you can skip them. You will be monitored for a period of 3 years.
A detailed overview of the course of the study can be found in the diagram in Appendix 1.

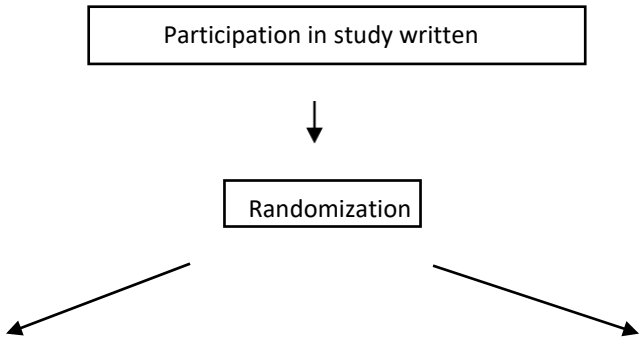
Radiation treatment
This treatment is performed by using stereotactic radiotherapy (SBRT). SBRT is a specialized, technologically advanced type of external beam radiation therapy that localizes a high dose of radiation to the metastasis. Due to the high precision, the healthy tissues in the vicinity are spared and the patient has little chance of side effects. SBRT is performed every other day with a maximum of 3 treatments per week. If different metastases are present, they will be irradiated one after the other on the same days. We aim to treat each metastasis in 3 times, but if necessary, the number of sessions can be extended to 7 times and this will depend on the dose calculations. If the prostate and seminal vesicles have not been treated in the past, you will also receive radiation treatment in 5 sessions. If the prostate and seminal vesicles have been treated before, but a local relapse needs to be treated, 35 radiation sessions will follow. The irradiation takes about 30 minutes at a time. You will not see or feel the radiation. You do not need to be admitted to hospital for

radiotherapy.

Surgery
Which surgical technique is used is determined by the surgeon according to which approach would yield the best results. This also depends on the location and extent of the metastases. If possible, minimally invasive procedures are preferred. These are procedures in which a smaller incision is made in the skin than in classic surgery.

Systemic therapy
If, as part of this study, you receive treatment with a subsequent line of systemic therapy (group A), it will be decided at a multidisciplinary meeting which systemic therapy you will receive exactly.

Study overview



Group A

Active follow-up or treatment with next-line systemic therapy

Group B

Metastasis-directed therapy with continuation of current systemic treatment

Course of treatment:

For examinations	Consultation and clinical examination Blood test Staging by means of PSMA PET-CT scan **Filling out questionnaires**
Randomization	Group A: Active follow-up or treatment with next line systemic therapy Group B: metastasis-directed therapy with continuation of current systemic treatment
Metastasis Courts Therapy	SurgeryRadiotherapy: +/- 3-7 radiation

	treatments, max 3x/week
Month 1	Standard follow-up + blood test + PSMA PET-CT every 6 months + **completion of questionnaires on M1, M6, M12, M18 and M24**
Month 3 and then every 3 months	

Bold **text** indicates what is 'extra' in study participation compared to the standard treatment outside the study.

5. Will I benefit from the study?

In this study, we will investigate whether we can extend the patient's lifespan by means of metastasis-directed therapy. In any case, the study will provide useful data for other patients in the future.

6. What are the potential risks and inconveniences of participating in the study?

6.1. What are the possible side effects?

All therapies have both known and unpredictable side effects. Although previous studies have shown that the various potential therapies in the study are generally well tolerated, it is possible that you will experience side effects.

The possible side effects of the treatment depend on the chosen technique (surgery versus radiotherapy) and the localization of the metastasis(s). These will be discussed thoroughly with you on an individual basis so that a correct assessment of the risks and potential side effects can be made by the patient. Every patient who will undergo surgery will be seen beforehand by an anaesthetist who will discuss all the risks of the operation with you.

The possible side effects of the systemic treatment are due to the expected pharmacological effects of the treatment in question. These side effects will be discussed with you thoroughly, if applicable.

6.2. What are the possible risks or inconveniences of the examinations during the study?

Disadvantages of participating in this study are:

- The time you lose filling out questionnaires (minus 10 minutes at a time).

It is also possible that other risks and inconveniences may occur that are currently unknown. It is therefore very important to report any new health complaint to the physician-investigator as soon as possible, regardless of whether you think the complaint is related to the study or not.

6.3. Can I take other medicines during the study?

Do not hesitate to ask your researcher for more information about the use of other medicines and dietary supplements.

6.4. Can my partner become pregnant during the study?

During the study, it is necessary that adequate contraception is used during heterosexual contacts, because of the possible adverse effects of the treatment on the unborn child. In the unlikely event that a pregnancy does occur, we wish to follow up on the pregnancy, with the consent of you and your partner. The necessary documents will be provided for this.

7. What if something goes wrong during the study?

Even if there is no fault, the sponsor is liable for the damage you suffer that is directly or indirectly related to your participation in the study. The client has taken out insurance for this liability (with "FAULTLESS LIABILITY") (Ref. 1). A copy of the insurance certificate can be obtained from the investigator or study staff.

If you (or your heirs) wish to be compensated for the damage you incur as a direct or indirect result of your participation in the study, you must inform the investigator or study staff as soon as possible.

If the investigator believes that a link between new or worsened health complaint(s) and the study is possible, he/she will report this to the sponsor of the study. The client will then immediately file a declaration with his insurance company. If the company deems it necessary, it will appoint an expert to check whether there is a link between your reported health complaint(s) and the study. The insurance does not cover the natural evolution of your disease/condition or the known side effects of the treatment that you would have received without participating in the study (this is your standard treatment).

If you find it necessary or in case of disagreement with the investigator or with the insurance company's expert, you or your heirs can contact the insurer or, if necessary, summon them. Contact details can be found on the cover page of this form.

8. What if other treatments or new information about the IMP become available during the study?

In the course of the study, new important information may become available, which could influence your decision to participate (further). For example, other treatments for your disease/condition or important new information about the IMP may become available. It is the duty of the investigator to discuss this new information with you and to give you the opportunity to review your participation in the study.

If you decide to end your participation in the study or if you are no longer able to participate, your investigator will ensure that you continue to receive the best possible treatment.

9. Can my participation in the study end early?

As discussed in detail later in this section, your participation in the study may end prematurely if

- you decide to withdraw your consent,
- the investigator decides to stop your participation in the study, or
- other agencies interrupt or terminate the study.

In any case, if you stop participating in the study early, the investigator will discuss your further medical care with you. The client can continue to store and use data that was already collected

before the termination of your participation. This is intended to avoid a misinterpretation of the study results (as described in section 12.4, page 11).

If you experience an adverse reaction at the time you stop taking the IMP, the investigator may contact you afterwards to check whether the side effect has disappeared or not after your participation in the study has ended.

If you experience a new side effect after finishing your participation in the study, you may contact the investigator and ask for follow-up.

9.1. You decide to withdraw your consent

You have the right to withdraw your consent without giving a reason. However, for your own safety, you must inform the investigator of your decision. Even though it is not mandatory, it may be useful for the researcher and the sponsor to know the reason for your decision (e.g. side effects, too many trips, etc.).

If you withdraw your consent, it means that you decide to stop

- treatment with the IMP, and
- all consultations and studies related to the study.

Please discuss with the investigator the practical side of discontinuing your participation (depending on your situation), including your further follow-up.

In any case, no new data will be provided to the client.

If your biological samples (e.g. blood samples, urine samples) have already been used or tested before the withdrawal of your consent, the sponsor still has the right to use the results of those tests.
Also, your biological samples that were collected (but not yet tested) before withdrawing your consent, and the data obtained from them, can still be used by the client. You can ask for these samples to be destroyed. To avoid an incorrect interpretation of the study results, this can be postponed until the end of the study.

If you have signed an additional consent form for the use of your samples in future research and you do not withdraw this additional consent, your samples can still be used for that study.

9.2. The investigator decides to stop your participation in the study

The investigator may terminate your participation in the study because

- it's better for your health,
- he/she experiences that you are not following the instructions given to the participants, or
- there is another reason that will be explained to you.

9.3. Other bodies may interrupt or terminate the study

The sponsor and the competent Belgian health authorities may interrupt or terminate the study,

- because the information collected shows that the IMP is not working well enough (does not provide sufficient improvement in the health of the study participants),
- because the IMP causes more (serious) side effects than expected, or
- for any other reason that will be explained by the authority concerned.

10. What treatment will I receive after participating in the study?

In all situations where participation in the study is discontinued, as well as when the study is completed as scheduled, your investigator will examine your health and prescribe you the best treatment available. Stopping your participation in this study or not participating in this study will have no impact on the course of your treatment and your relationship with the physician-investigators. They will give you the best possible treatment in all cases.

11. Will my participation in the study incur additional costs?

The treatments and examinations that are study-specific will be paid for by the sponsor and will not be charged to you. The treatments and examinations that are part of your standard treatment will be charged to you or your health insurance fund (Belgian social security). Please contact the study staff for more details if you are not affiliated with a health insurance fund (Belgian social security).

12. What data will be collected about me during the study and what will happen to it?

12.1. What data will be collected and processed during the study?

The personal data collected and processed are about your health and medical condition, including your medical history, some of your background information (e.g. your age, gender and ethnic origin) and the results of the study examinations.

12.2. How will the researcher handle my personal data?

The researcher is bound by professional secrecy when collecting and processing your data.

This means that he/she will never reveal your identity, not even in a scientific publication or a lecture, and that he/she will encrypt your data (i.e. replace your identity with an identification code in the study) before sending it to the sponsor.

As a result, the investigator, and the study staff under the responsibility of the investigator, will be the only ones who will be able to link your identity to the data transmitted during the study, with the exceptions mentioned under 12.6.

The data that the client receives will therefore not be able to identify you.

12.3. What will happen to the information collected during the study?

Your participation in the study means that your personal data

- Collected by the researcher, and
- Used in coded form by the sponsor of the study.

The researcher and the sponsor may only use the encrypted personal data for research purposes in connection with scientific publications in the context of the study in which you participate.

If wider use of the encrypted data is planned, this will be stated below.

In addition, the sponsor can grant external researchers (who are not involved in this study) access to the encrypted data. If an external investigator wishes to use the data in research that is not yet described in this document, this research must be approved by an Ethics Committee. If your encrypted data is sold, you will not be compensated.

12.4. How will my data be processed?

Your study data will be processed in accordance with the General Data Protection Regulation (GDPR) (Ref. 2) and the Belgian Data Protection Act of 30 July 2018 (Ref. 3). The client is responsible for this.

The reason why we are allowed to process your personal data is that we conduct scientific research and that **you have given your consent**.

The processing of your personal data is necessary in order to achieve the scientific research purposes as described herein. Conducting academic research is one of UZ Leuven's statutory assignments as commissioner. As a university hospital affiliated with KU Leuven, UZ Leuven must support science and education in the public interest. UZ Leuven would like to clarify that the necessity of the processing for the purpose of conducting scientific research and this as a task in the public interest, is the legal ground for authorisation on the basis of which UZ Leuven processes your data in the context of this research. In addition, UZ Leuven is subject to specific legal obligations that may make the processing of your data necessary in the context of safety reporting (such as, for example, reporting side effects to supervisory government authorities).

12.5. Can I access my data collected and processed during the study and rectify it?

You have the right to ask the investigator what data is collected about you and what it is used for in this study.

You have the right to:

- Access and review this data
- Ask for correction if they are incorrect.

Regarding the PSMA PET-CT scan performed as part of the study, the patient can only access and review this data after blinding this scan. This is to prevent the results of the study from being misinterpreted. Please ask your researcher when you can access this data.

12.6. Who other than the researcher and his staff has access to my personal data?

In order to check the quality of the study, your non-encrypted personal data or information relevant to this study from your medical file may be inspected by people other than the study staff. This inspection takes place under the supervision of the investigator and these persons are bound by professional secrecy or by a confidentiality agreement. This may involve:

- Personnel designated by the client (MONITORS and AUDITORS) and people or organisations who provide services to or work with the client. However, they will never pass on your name and contact details to the client.
- inspectors from the competent health authorities from all over the world
- an independent audit group
- persons appointed by the Ethics Committee.

If necessary for the study, the encoded study data may be sent to other countries within and outside the European Union (EU) and may be reviewed by:

- staff (other than inspectors) of the competent health authorities of Belgium (Federal Agency for Medicines and Health Products, FAMHP) or other countries within and outside the EU,

- the Belgian Ethics Committee(s),
- external researchers,
- the sponsor of the study, personnel designated by the sponsor and people or organisations that provide services to or collaborate with the sponsor, and/or
- companies from the client's group in Belgium and in other countries within and outside the EU.

European regulations and Belgian data protection laws impose restrictions on the transfer of data to non-EU countries. The sponsor must always ensure that your encrypted study data is equally protected when transferred to a non-EU country. If the sponsor enters into a data protection agreement for this purpose, a copy of this agreement can be obtained from the researcher.

You can always contact your researcher for more information about such transfers.

12.7. What will happen to the results of the study?

After completion of the study, a description of the results of the study will be published in specialized medical journals. A copy of the scientific publication is available from the investigator or study staff. A description of the study will also be available on https://www.clinicaltrialsregister.eu and/or https://www.clinicaltrials.gov. With the help of the study number that you will find on the cover page of this document, you can consult this study. Within 1 year of study completion, the websites will include a summary of the results (Ref. 4).

These websites or publications will not contain any information that can be used to identify you.

12.8. Will my data be used for purposes other than the study in which I am participating?

The results of the study will only be used to answer the scientific questions in this study.

12.9. How long will my data be stored?

At the end of the study, your coded data will be kept for at least 25 years (Ref. 5) to ensure the validity of the study. This will also be the case if you stop participating in the study prematurely.

13. Which biological samples will be collected from me during the study and what happens to them?

Biological samples are samples of human body material (e.g. blood, tissue, urine, stool, etc.). The collection of biological samples is not applicable to this study. The blood tests that are performed during the course of the study are part of the standard treatment of patients with metastatic prostate cancer. These blood samples are destroyed after the standard analyses.

14. Who reviewed and approved the documents relating to the study?

The study documents were reviewed by:

- the Belgian competent health authorities (FAMHP) or, if applicable, by the national competent health authorities of other EU Member States, and
- an independent Belgian Ethics Committee

The competent health authorities and the ethics committees have the task of protecting the persons participating in a study. The competent health authorities will ensure that the study is carried out in accordance with the applicable legislation.

You should not take their approval as an incentive to participate in the study.

15. What happens in case of accidental finds?

A result that happens to be found during the study and on top of the objectives is called a chance find. If this result may be important for your health or that of your blood relatives, the sponsor will inform the investigator about this. With your consent, the investigator will inform you and your treating physician of your results and the possible consequences. If necessary, the investigator and/or the attending physician will advise you on what to do.

CHAPTER II – INFORMED CONSENT

PARTICIPANT

REQUIREMENTS FOR YOUR PARTICIPATION IN THE STUDY:

- I declare that I have been informed about the purpose of the study, its duration and consequences, possible risks and inconveniences, the precautions I must take and what is expected of me, and that I have understood all this. My rights as a participant in a study have been explained to me and I have understood them.
- I have had enough time to think about it and talk about it with a confidant (e.g. friends, family, attending physician, etc.).
- I have had the opportunity to ask all the questions that came to my mind and I have received a satisfactory answer.
- I understand that I will participate in this study voluntarily and without being forced to do so and that I can stop participating in the study at any time
- I understand that data about me will be collected and treated confidentially.
- I understand that the conduct of this study by UZ Leuven serves the public interest and that the processing of my personal data is necessary for the conduct of this study.
- I understand that the client has taken out insurance in case I would suffer damage in connection with participation in this study.
- I understand that I will not incur any costs when participating in this study, except for the standard treatment of my disease.
- I consent to my treating physician(s) being informed of my participation in this study.
- I agree that I will not participate in another study at the same time without informing the investigator or study staff, and that they may refuse to participate for justified reasons.
- I understand that I must cooperate and follow the instructions of the investigator and of the study staff around the study.
- I understand that my participation in the study may be terminated without my consent if I require other treatment, do not follow the study schedule, have an injury related to the study, or for any other justifiable reason.
- I confirm that all the information I have about my medical history is correct. I understand that it may cause me harm if I fail to inform or point out possible exclusion criteria to the investigator.

I agree to participate in the study and I have received a signed and dated copy of all pages of this document.

Name and surname of the participant:.....

Datum (DD/MM/JJJJ):…… Participant's signature:.....

RESEARCHER

I, the undersigned researcher, confirm

- That the participant has been given the necessary information about the study orally, that the content has been explained to him/her and that he/she has been provided with an original signed version of this document.
- that I checked whether the participant understood the study.
- that I have given the participant enough time to think about his/her participation and to ask questions.
- that no pressure was exerted on the participant to agree to participate in the study.
- that I work in accordance with the ethical principles as stated in the most recent version of the "Declaration of Helsinki", the "Good Clinical Practice" and the Belgian law (Ref. 6).

Researcher's surname and first name:.....

Datum (DD/MM/JJJJ):…… Investigator's signature:.....

GLOSSARY

FAMHP: Federal Agency for Medicines and Health Products

DPA: The Belgian Data Protection Authority ensures that personal data is used and protected with care, and that your privacy is guaranteed in the future.

INSURANCE WITH "NO-FAULT" LIABILITY:

The sponsor is liable for any injury or damage to the participant that is directly or indirectly related to the study. You do not need to prove an error for this.

MONITOR at AUDITOR:

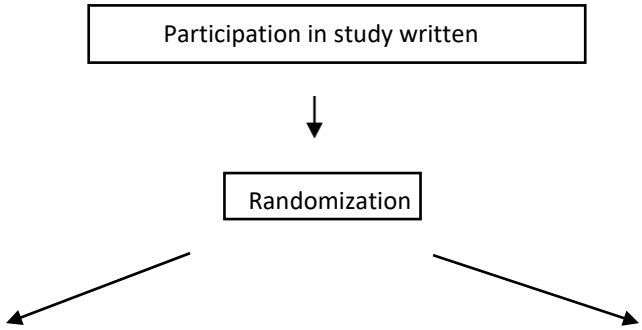
Both the monitor and the auditor work for the client. The monitor ensures continuous quality control throughout the course of the study. The auditor conducts an investigation after the study has been completed. They check whether the study is/was conducted according to the protocol, whether the reported data is reliable and whether the study is in accordance with the applicable laws.

CREDENTIALS

1. This is in accordance with Article 29 of the Belgian law of 7 May 2004 on experiments on human beings and the applicable Royal Decrees.
2. General Data Protection Regulation No 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC.
3. Belgian law of 30 July 2018 on the protection of natural persons with regard to the processing of personal data.
4. In accordance with Chapter 4.3. of the Commission Directive : Guidelines for the placement and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 - 2012/302/03.
5. In accordance with Article 58 of Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use and repealing Directive 2001/20/EC.
6. Belgian law of 7 May 2004 on experiments on human beings and the applicable royal decrees.

CHAPTER III – ADDITIONAL INFORMATION

Appendix 1: Study overview



Group A

Active follow-up or treatment with next-line systemic therapy

Group B

Metastasis-directed therapy with continuation of current systemic treatment

Course of treatment:

For examinations	Consultation and clinical examination Blood test Staging by means of PSMA PET-CT scan **Filling out questionnaires**
Randomization	Group A: Active follow-up or treatment with next line systemic therapy Group B: metastasis-directed therapy with continuation of current systemic treatment
Metastasis Directed Therapy	SurgeryRadiotherapy: +/- 3-7 radiation treatments, max 3x/week
Month 1	Standard follow-up + blood test + PSMA PET-CT every 6 months + **completion of questionnaires on M1, M6, M12, M18 and M24**
Month 3 and then every 3 months	

Bold **text** indicates what is 'extra' in study participation compared to the standard treatment outside the study.