Study title: **Prediction of Response related to IMmune age T cell fitness in Elderly patients with relapsed and refractory multiple myeloma**

Study sponsor: *Dr Marie VERCRUYSSEN, Haematology Department, Jules Bordet Institute, HUB.*

Research organisation*: Jules Bordet Institute, HUB-ULB, Rue Meylemeersch 90, 1070 Anderlecht, Belgium*

Medical Ethics Committee*: Jules Bordet Institute, HUB-ULB, Rue Meylemeersch 90, 1070 Anderlecht, Belgium*

Local investigators:

Dr Marie VERCRUYSSEN, principal investigator, *Haematology Department, Jules Bordet Institute, HUB, marie.vercruyssen@hubruxelles.be*

Dr Ahmet-Fatih KARADAG, postgraduate researcher, *Haematology Department, Jules Bordet Institute, HUB,*
ahmet-fatih.karadag@hubruxelles.be

I Key information to help you decide whether to participate

Introduction

You are invited to take part in a clinical study designed to better understand the role of the immune system in the response to innovative immunotherapy treatments for multiple myeloma. The aim is *to assess how certain characteristics of T lymphocytes, key cells of the immune system, may influence the effectiveness of treatments and the occurrence of side effects in patients aged over 65.*

Participation in this study will in no way affect the treatment you will receive, nor the expected outcomes that have been explained to you by your haematologist.

Before you agree to take part, we invite you to familiarise yourself with the implications of the study in terms of organisation, benefits and potential risks, so that you can make an informed decision. This is known as giving 'informed consent'.

Please read these few pages of information carefully and ask any questions you may have to the investigator or their representative. This document consists of three parts: the essential information for your decision-making, your written consent, and supplementary information (appendices) which provide further details on certain aspects of the basic information.

If you take part in this clinical trial, you should be aware that:

- This clinical trial has been approved by several ethics committees, including the HUB-ULB committee.
- Your participation is voluntary and must remain free from any coercion. It requires the signing of a document expressing your consent. Even after signing it, you may withdraw from the study by informing the investigator. **Your decision not to participate or to withdraw from the study will have no impact on the quality of your care or on your relationship with the investigator.**
- The data collected during the study is confidential, and your anonymity is guaranteed when the results are published.
- Insurance has been taken out in case you suffer any harm related to your participation in this clinical trial.
- You will not be charged for the additional blood sample required for this study.
- You can always contact the investigator or a member of their team if you require further information.

These points are detailed in the appendix 'Rights and protection of clinical research participants'.

Objectives and description of the study protocol

We invite you to take part in a clinical trial investigating the role of the immune system in the response to innovative immunotherapy treatments for multiple myeloma. This trial is expected to include around 30 participants

The principle behind immunotherapy treatments is based on stimulating each patient's immune system to enable it to eliminate cancer cells. The aim of this study is to better understand how certain characteristics of T lymphocytes (immune system cells) influence the response to recent treatments such as CAR-T cells and bispecific antibodies, as well as the occurrence of side effects ina population of patients aged over 65 who have relapsed or refractory multiple myeloma and who are eligible for immunotherapy treatments such as CAR-T (cilta-cel) and/or bispecific antibodies (Teclistamab, Elranatanab, Talquetamab).

As you fall into this category of patients, your haematologist has therefore suggested that you take part in this study, which will not alter the treatment or outcomes that have been explained to you in any way. Your participation will mainly involve the collection of anonymised clinical data and a blood test prior to the start of your treatment. A geriatric assessment and a bone density scan will also be offered. You will be monitored according to your usual consultation schedule, with standard assessments following the start of treatment.

Study procedure

Your participation in the study will last for 3 months after the start of treatment. Treatment monitoring will be carried out in accordance with standard practice.

Risks and disadvantages

A: Interactions with tests, treatments and examinations

The study-specific procedures mainly consist of a blood test, a clinical assessment and a medical imaging scan. No other major study-related constraints are expected, and your medical care will remain in line with standard practice.

It is important that any new health issues are reported to the investigator, regardless of how likely you think they are to be related to the study.

C: Risks associated with clinical trial procedures

The **blood sample** (approximately 4 to 6 ml of blood) required to analyse **your immune system** may (rarely) cause pain, bleeding, bruising or a localised infection at the site of the blood draw. Similarly, some participants may experience dizziness or even fainting during the procedure. The staff performing the blood draw will do their utmost to minimise these discomforts.

A bone densitometry (DEXA) scan may be carried out to assess muscle and/or bone mass. This scan is quick, painless and non-invasive. It involves lying down for a few minutes whilst a machine measures your body composition.

Bone densitometry uses a very low dose of X-rays, comparable to that of a standard X-ray. The associated risks are therefore very low. No side effects or impact on daily life are expected following this test

The geriatric assessment will enable us to examine all your body's functions in order to detect any potential frailties before starting your treatment.

Benefits

We do not expect your participation in this study to provide you with any personal benefits. You should understand that your participation in this study will enable us to better understand the role of the immune system and, consequently, to offer better treatments in the future.

Withdrawal from the study

Your participation is voluntary and you have the right to withdraw from the study for any reason, without having to give a reason. It is also possible that the investigator may withdraw you from the

study because they believe it is in the best interests of your health or because they observe that you are not complying with the instructions given to participants.

Finally, there are occasions when the relevant ethics committees – such as the HUB-ULB Ethics Committee – which initially approved the study, or the sponsor, may suspend the study for medical reasons.

Contact

If you require further information, or if you have any problems or concerns, you can contact the investigator, **Dr Marie VERCRUYSSEN,** or a member of her research team, **Dr Ahmet KARADAG,** on the following telephone number (+32 251 30 29).

For the Cliniques universitaires Saint-Luc (Institut Roi Albert II), you can contact **Prof. Marie-Christiane VEKEMANS** on 02 764 12 00.

For Saint-Pierre University Hospital, you can contact Dr Nicolas CILLA on 02 535 31 11.

If you have any questions regarding your rights as a participant in a clinical trial, you can contact your institution's participant rights ombudsman on +32 (0)2 541 35 11 or by email at mediation-ombudsdienst@hubruxelles.be. If necessary, the ombudsman can put you in touch with the local ethics committee.

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II Informed consent

Participant

I declare that I have been informed about the nature of the study, its purpose, its duration, the potential benefits and risks, and what is expected of me. I have read the information sheet and the appendices to this document.

I have had sufficient time to think about it and discuss it with a person of my choice, such as my GP or a family member.

I have had the opportunity to ask any questions that came to mind and have received satisfactory answers to my questions.

I understand that my participation in this study is voluntary and that I am free to withdraw from the study at any time without this affecting my relationship with the healthcare team responsible for my care.

I understand that data concerning me will be collected throughout my participation in this study and that the investigator and the study sponsor guarantee the confidentiality of this data in accordance with applicable European and Belgian legislation.

I consent to the processing of my personal data in accordance with the terms set out in the section on confidentiality guarantees (see Appendix: Participant Rights and Protection). I also consent to the transfer and processing of this data in countries other than Belgium.

I agree / do not agree (delete as appropriate) that the research data collected for the purposes of this study may be processed at a later date, provided that such processing is limited to the context of this study in order to improve our understanding of the disease and its treatment.

I agree / do not agree (delete as appropriate) that the sponsor may retain samples of biological material collected during the study for 5 years for the purposes of further research, provided that such research is limited to the context of this study.

I agree that my GP or other specialist doctors responsible for my care may be informed of my participation in this clinical trial.

As described in the section entitled ‘Incidental findings’, it is possible that incidental findings may be made which could be important for your health or the health of your relatives.

I agree/do not agree (delete as appropriate) that the investigator should keep me informed (directly or via my GP) of this result.

I have received a copy of the participant information sheet and the informed consent form. Surname, first name, date and signature of the volunteer.

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Legal representative

I declare that I have been informed that I am being asked to make a decision regarding the person I represent’s participation in the clinical trial in their best interests and taking into account their likely wishes. My consent applies to all items included in the participant’s consent form.
I have also been informed that as soon as the clinical situation permits, the person I represent will be informed of their participation in a clinical trial and will then be free to consent to continuing their participation or to withdraw from it by signing or refusing to sign this consent form.

I have received a copy of the information for participants and the informed consent form.

Surname, first name and relationship to the person represented

Date and signature of the legal representative.

Witness / Interpreter

I was present throughout the entire process of informing the participant and I confirm that information on the objectives and procedures of the study was provided adequately, that the participant (or their legal representative) appeared to have understood the study, and that consent to participate in the study was given freely.

Surname, first name and qualification of the witness / interpreter:

Date and signature of the witness / interpreter.

Investigator

I, the undersigned, _____, the investigator, confirm that I have provided the necessary information about the study orally and have provided a copy of the information sheet to the participant.

I confirm that no pressure has been exerted on the participant to agree to take part in the study and that I am prepared to answer any further questions, if necessary.

I confirm that I am working in accordance with the ethical principles set out in the latest version of the 'Declaration of Helsinki', 'Good Clinical Practice' and the Belgian Act of 7 May 2004 on clinical trials involving human subjects.

Surname, first name, date and signature of the investigator's representative

Surname, first name, date and signature of the investigator

III Appendix: Participants' rights and protection

1: Further information on the organisation of the study

Your participation in this study will not result in any changes to your usual medical care. The treatment offered to you will be decided by your doctor in accordance with current guidelines and independently of your participation in the study.

2: Further information on the protection and rights of participants in a clinical trial

Ethics Committee

This study has been reviewed by an independent Ethics Committee, namely the Ethics Committee of the Brussels University Hospitals (HUB) for the Jules Bordet Institute of the HUB, which has issued a favourable opinion. The local Ethics Committee is responsible for approval at their centre for the Saint-Luc University Clinics (King Albert II Institute) and for the Saint-Pierre University Hospital. The role of Ethics Committees is to protect people taking part in a clinical trial. They ensure that your rights as a participant in a clinical trial are respected, that, based on current knowledge, the balance between risks and benefits remains favourable to participants, and that the trial is scientifically sound and ethical.

The Ethics Committees issue their opinions on this matter in accordance with the Belgian Act of 7 May 2004.
Under no circumstances should you regard the Ethics Committee's favourable opinion as an incentive to take part in this study.

Voluntary participation

Before signing, please feel free to ask any questions you consider necessary. Take the time to discuss this with someone you trust if you wish.

Your participation in the study is voluntary and must remain free of any pressure: this means that you have the right not to participate or to withdraw without giving a reason, even if you had previously agreed to take part. Your decision will in no way affect your relationship with the investigator or the quality of your future medical care.

If you agree to take part in this study, you will sign the informed consent form. The investigator will also sign this form, thereby confirming that they have provided you with the necessary information about the study. You will receive your own copy.

For your own safety, it is advisable to inform the investigator if you have decided to withdraw from the study.

Costs associated with your participation[1]

If you decide to take part in this study, there will be no additional costs to you or your health insurer for the additional tests carried out to analyse your blood's immune profile. The blood sample taken for routine tests will be covered in the usual way, in part by your health insurance provider. The additional analyses of your immune profile carried out as part of this study will be covered by a grant allocated by the Haematology Department at the HUB.

Confidentiality guarantee

Your participation in the study means that the investigator will collect data about you and that the study sponsor will use this data for research purposes and in scientific and medical publications.

The processing of your personal data during this study is authorised, as it is necessary for scientific purposes.

[1] Please refer to BAREC's guidelines on participant reimbursement on their website https://barec.be/.

Your data will be processed in accordance with the General Data Protection Regulation (GDPR) and Belgian legislation on the protection of natural persons with regard to the processing of personal data. Dr Marie Vercruyssen will be responsible for processing your data.

You have the right to ask the investigator what data is being collected about you and how it will be used in the context of the study. This data relates to your current clinical condition, as well as certain aspects of your medical history, the results of tests carried out as part of your standard healthcare, and, of course, the results of tests required by the protocol. You have the right to access this data and the right to request corrections should it be incorrect[2] .

The investigator has a duty of confidentiality regarding the data collected.

This means that they undertake not only never to disclose your name in any publication or at a conference, but also to pseudonymise your data (replacing your identity with an identification code within the study) before passing it on to the manager of the database, Dr Ahmet-Fatih KARADAG, Department of Haematology at the Jules Bordet Institute.

The investigator and his team will therefore be the only ones able to link the data transmitted throughout the study to your medical records[3] .

The personal data transmitted will not contain any combination of elements that would allow you to be identified[4] .

For the research data manager appointed by the sponsor, the data transmitted does not allow you to be identified. The sponsor is responsible for the collection of data gathered by all investigators participating in the research, its processing and its protection in accordance with the requirements of Belgian law on the protection of privacy.

To verify the quality of the study, your medical records may be examined by individuals bound by professional confidentiality and appointed by the HUB-ULB Ethics Committee, the study sponsor or an independent audit body. In any event, this review of your medical records may only take place under the responsibility of the investigator and under the supervision of a member of staff designated by them.

The (pseudonymised) research data may be shared with Belgian or other regulatory authorities, the relevant ethics committees (including the HUB-ULB Ethics Committee), other investigators and/or organisations working in collaboration with the sponsor.

It may also be shared with other sites of the sponsor in Belgium and in other countries where data protection standards may differ or be less stringent. As explained above, the data shared is pseudonymised[5] .

Your consent to participate in this study therefore also implies the use of your pseudonymised medical data for the purposes described in this information document and its transmission to the persons and bodies mentioned above.

The sponsor undertakes to use the data collected solely for the purposes of the study in which you are participating.

The sponsor will use the data collected in the context of the study in which you are participating but also wishes to be able to use it in the context of other research concerning the same condition as yours. Any use of your data outside the context described in this document may only be carried out following approval by the HUB-ULB Ethics Committee.

If you withdraw your consent to participate in the study, in order to ensure the validity of the research, the data pseudonymised up to the time of your withdrawal will be retained. No new data may be transmitted to the sponsor.

If you have any questions regarding the processing of your data, you may contact your investigator. Your hospital's Data Protection Officer is also available to assist you.
Their contact details are as follows: dpo@hubruxelles.be.

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[2] These rights are guaranteed to you by the General Data Protection Regulation (GDPR), by the Belgian legislation of 30 July 2018 on the protection of natural persons with regard to the processing of personal data, and by the Act of 22 August 2002 on patients' rights.

[3] For clinical trials, the law requires this link to be retained in your file for 25 years.

[4] The database containing the study results will therefore not contain any combination of details such as your initials, your gender and your full date of birth (dd/mm/yyyy).

[5] The sponsor therefore undertakes to comply with the requirements of the General Data Protection Regulation (GDPR) and Belgian legislation on the protection of individuals with regard to the processing of personal data.

Finally, if you have a complaint regarding the processing of your data, you may contact the Belgian supervisory authority responsible for ensuring compliance with the fundamental principles of personal data protection:

The Belgian supervisory authority is called:
The Data Protection Authority (APD)
Rue de la Presse 35,
1000 Brussels
Tel. +32 2 274 48 00
Email: contact@apd-gba.be
Website: https://www.autoriteprotectiondonnees.be

What will happen to the samples taken during the study?

The sponsor of this study undertakes to use the samples strictly within the context described in this section.

1) Samples collected during the study
The coding procedure for your biological samples is the same as that used for your personal data. Samples sent to the sponsor or to organisations working in collaboration with the sponsor will therefore only be labelled with your study-related identification code. The sponsor is responsible for ensuring the traceability of your biological samples.
The managers of these samples, Dr Julie Smet and Dr D'Otreppe, of the Brussels University Hospitals Laboratory, undertake to use them for clinical research purposes and to destroy them at the end of the specified storage period.
The biological sample collected is considered a 'donation', and you should be aware that, as a matter of principle, you will not receive any financial benefit (royalties) in connection with the development of new therapies derived from the use of your biological sample, which may have commercial value.

If you withdraw your consent to participate in the study, you may contact the investigator to have the unused portion of your sample(s) destroyed. The results obtained from your samples prior to the withdrawal of your consent remain the property of the study sponsor.

2) Residual samples

The sponsor must use these in the context of the study in which you are participating, in accordance with the description above. Your residual samples will be destroyed once the analyses have been carried out. In principle, this will be within 5 years.

As scientific progress in this field is ongoing, the sponsor wishes, with your consent, to retain your residual biological samples for 5 years. These samples will be used in future research – outside the study in which you are participating – aimed at better understanding the disease, its treatment and responses to that treatment. Any study outside the context described in this document may only take place following approval by a HUB-ULB ethics committee.

Incidental findings

If, by chance and in addition to the study's objectives, a finding is discovered during the study that may be important for your health or that of your relatives with whom you share a biological link (known as an 'incidental finding'), the sponsor will inform the investigator. With your consent, the investigator will inform you and your treating doctor of your results and their potential implications. If necessary, the investigator and/or your treating doctor will advise you on the next steps. You may agree or refuse to be informed of this by indicating your preference on consent form P.X.

No-fault insurance

Any participation in a clinical trial involves a risk, however small. The sponsor assumes liability, even in the absence of fault, for any harm caused to the participant (or, in the event of death, to their beneficiaries) that is directly or indirectly related to their participation in the research. The sponsor has taken out insurance to cover this liability[6] .

You are therefore asked to report any new health problems to the investigator. He or she will be able to provide you with further information regarding possible treatments..

If the investigator considers that a link with the study is possible (as the insurance does not cover the natural progression of your illness or the known side effects of your usual treatment), he or she will inform the study sponsor, who will then initiate the insurance claim procedure. The insurer will appoint – if it deems it necessary – an expert to assess the link between your new health problems and the study.

In the event of a disagreement with either the investigator or the expert appointed by the insurance company, and whenever you deem it appropriate, you or – in the event of your death – your beneficiaries may sue the insurer directly in Belgium (Brussels University Hospitals).

The law provides that the insurer may be summoned either before the court of the place where the event giving rise to the damage occurred, or before the court of your place of residence, or before the court of the insurer's registered office.

[6] In accordance with Article 29 of the Belgian Law on Human Experimentation (7 May 2004)