Positron emission tomography with innovative laboratory techniques for improved risk and disease assessment in myeloma

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haematopoietic neoplasms (excl leukaemias and lymphomas)
Study type	Observational invasive

Summary

ID

NL-OMON53692

Source
ToetsingOnline

Brief title
IMMPROVED

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
Myelomatosis

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Antwerpen

Source(s) of monetary or material Support: FWO-TBM

Intervention

Keyword: FDG PET/CT, MRD, Multiple myeloma, WES

Outcome measures

Primary outcome

The primary endpoint of this study is to evaluate the prognostic value of FDG-PET combined with NGF in patients achieving VGPR or better after induction chemotherapy and ASCT and before lenalidomide maintenance therapy. We hypothesize that only patients who have no evidence of disease on both NGF and FDG-PET have a durable response with a 2y PFS of 90% compared to 50% in pts who have evidence of disease on at least one modality. PFS is defined as the time from achieving >= VGPR and confirmation of absence of MRD (landmark) to first documentation of objective progressive disease or death due to any cause, whichever occurs first. The <10-5 MRD level is used to define BM-NGF MRD-negativity. A Deauville score=3 threshold will be used to define FDG-PET MRD-negativity, but alternatives will also be evaluated (other DS, more quantitative measures like SUV)

Secondary outcome

The secondary endpoint is to implement WES and Radiomics at baseline to improve risk-stratification.

Study description

Background summary

Multiple myeloma (MM) is defined by a malignant proliferation of plasma cells in the bone marrow (BM). It is the second most common hematological malignancy after lymphomas and accounts for 1% of all cancers. According to data from the Belgian Cancer Registry, each day two patients receive a diagnosis of MM in Belgium.
Currently, newly diagnosed MM (NDMM) patients who are fit for intensive treatment can obtain durable clinical responses, including complete responses (CR). Nevertheless, there is still a population of high-risk NDMM patients that fail to achieve durable responses. The prognosis of these patients, representing 20% of the patients, is particularly grim, with a median overall survival (OS) of only 2 years compared to 7-10 years for the overall transplant-eligible group. Upfront identification of this high-risk population is critically important, because these patients may benefit from more intensified treatment approaches or from treatment with novel agents.
Combination of these techniques, FDG-PET/CT, CXCR4-PET/CT, NGF and WES, could help identify these high-risk vs low-risk patients and could help in defining patient specific treatment strategies

Study objective

The aim of this project is to validate 3 novel biomarkers (FDG PET/CT, WES and NGF). The utilization goal is to implement these biomarkers afterwards in clinical practice to rationalize treatment strategies.
The primary objective is to validate the use of FDG-PET/CT imaging combined with BM-NGF to refine the definition of MRD after ASCT; if validated, this new biomarker combination could be used for a more risk-adapted approach after ASCT to determine which pts might benefit most from lenalidomide maintenance and to shorten the duration of maintenance in pts with persistence of MRD-negativity.
As secondary objective, we will explore the use of PET radiomics and WES prior to the start of treatment to better discriminate between high-risk and standard-risk pts, which is important to shift from the current *one-size-fits-all* therapeutic approach to a more risk-adapted approach

Study design

Observational study - no intervention.

This study includes newly diagnosed multiple myeloma patients who will receive standard of care. This standard of care includes induction chemotherapy followed by autologous stem cell transplantation (ASCT) followed by lenalidomide maintenance therapy. Prior to the start of treatment, all patients will undergo a whole body FDG-PET/LDCT. An aliquot of the BM sample will be used for WES. Patients who achieve at least a very good partial response (VGPR) according to the IMWG response criteria, will start lenalidomide maintenance therapy 3 months after ASCT. Prior to the start of maintenance, PET imaging with FDG will be repeated when positive at baseline. MRD status will be

defined based on NGF (Euroflow protocol) on BM aspirate before and after 1 and 2 years of maintenance therapy. During maintenance therapy, patient will undergo follow-up visits. These visits will depend on the center/treating doctor, but should be recorded in the eCRF at least once every 3 months. These visits will include a clinical examination, biochemical analysis, as well as serum and urine electrophoresis. In the absence of toxicity, maintenance treatment will be continued until biochemical or clinical progressive disease according to IMWG criteria, irrespective of the PET or NGF results.
If a patient shows relapse (PD) during lenalidomide maintenance therapy, a bone marrow examination will be performed and a bone marrow aspirate will be taken for WES-analysis.

In addition, patients can also be included after ASCT, and prior to the start of lenalidomide maintenance therapy. Remark: patients can only be included when a baseline FDG PET scan is available showing FDG avid disease (= at least 1 focal lesion DS4). WES and NGF data at baseline can be performed by using leftover bone marrow material (if leftover material is available). It is expected that no baseline CXCR4-PET scan will be available for this subgroup of patients.

Study burden and risks

As this is an observational study, no additional risks are associated with participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Transplant eligible newly diagnosed multiple myeloma based on current IMWG criteria and scheduled for induction therapy followed by autologous stam cell transplantation.
- Baseline 18F-FDG PET/CT scan should be performed. Prior to start of treatment, or within 7 days after the start. the scan should show FDG avid disease.
- WHO performance status 0-2 (WHO >2 can be allowed if due to underlying disease and after discussion with the physician)
- Age 18 years or older
- life expectancy > 12 months, based on clinical judgement.
- achieving at least VGPR after induction therapy and ASCT according to the standard IMWG response criteria.
- received at least one (28-day) cycle of lenalidomide as maintenance therapy after ASCT. No new therapy can be given until clinical relapse.

Exclusion criteria

- any physical or physiological condition that may affect adherence to the study protocol (severe claustrophobia, inability to lie still for 30 minutes)
- uncontrolled diabetes
- history or concomitant presence of any other malignancy, except for: non-melanoma skin cancer, carcinoma in situ of the cervix, any other effectively treated malignancy that has been in remission for >5 years or that is highly likely to be cured at time of enrollment.
- pregnant or breast feeding
- no informed consent
- participation in other (interventional) clinical trials without permission of the study team.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-11-2023
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	23-05-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL81867.029.22