In-house dual CAR T-cell therapy development

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To investigate the production of sufficient numbers of effective CAR/CCR T-cells with T-cells obtained from blood of MM patients.

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

Summary

ID

NL-OMON56725

Source
ToetsingOnline

Brief title
ID-CAR T trial

Condition

- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
Multiple Myeloma

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Stichting Life Science Made Better

Intervention

Keyword: blood sample collection, CAR-T cell production, Multiple Myeloma

Outcome measures

Primary outcome

We define effective production of CAR T-cells from patient blood as follows:

- Minimum expansion of 5-fold.

- >65% effective killing of myeloma cells

- 15-50% T cell transduction with a GMP-grade retroviral vector

- Viability of > 80 %

Successful: when >=4 out of 5 experiments per group meet these endpoints

Unsuccessful: when <4 out of 5 experiments per group meet these endpoints

Secondary outcome

n.a.

Study description

Background summary

B-cell maturation antigen (BCMA) chimeric antigen receptor (CAR) T-cell therapy has shown impressive results in patients with heavily pretreated multiple myeloma (MM).
However, relapses still occur, which may be explained by reduced target antigen expression on tumor cells and low persistence of CAR T-cells.
The Amsterdam UMC is currently developing CAR-T cell therapy for patients with MM. Laboratory research with healthy donor T-cells demonstrated that a CAR targeting BCMA, in combination with a CD38 chimeric costimulatory receptor (CCR), results in high affinity, efficient CAR T-cells with good persistence.
A next step to validate these findings is using T-cells of MM patients. It is reasonable to expect that MM patients will have reduced T-cell functionality either due to the disease itself, but especially due to previous treatment with drugs known to hamper T-cell function.

Study objective

To investigate the production of sufficient numbers of effective CAR/CCR T-cells with T-cells obtained from blood of MM patients.

Study design

Pre-clinical in vitro study.

Patient groups:
Group 1A: Triple refractory MM patients (n=5)

Group 2A: MM patients; treated with BsAbs either on treatment or within 3 months after discontinuation (n=5).

Group 1A and 2A are expected to be most challenging due to previous treatment. If showing efficacy in small scale (6 well-plate) (when >=4 out of 5 experiments meet the study endpoints), this will be extended to a patient scale (fully GMP-compliant closed-system process with the Lonza Cocoon) in vitro experiment (n=5 per group).

If CAR/CCR T-cell production fails (small or full scale, when <4 out of 5 experiments meet the study endpoints) with T-cells from patients described in group in 1A and/or 2A, it will be investigated in group 1B, 1C and/or 2B, again first small scale, if successful (again when >= 4 out of 5 experiments meet the study endpoints) also full scale.
- Group 1B: MM patients having received first line treatment only (n=5)
- Group 1C: Non-treated newly diagnosed MM patients (n=5)
- Group 2B: MM patients >3 months after BsAbs treatment discontinuation (n=5)

Study burden and risks

Patients will undergo extra blood sampling during a routine visit.
For the small scale experiment the quantity will be 50 ml. This amount is not harmful for the patient.

For the full scale experiment the quantity will be 200 ml. This amount may cause dizziness or a lower blood pressure in some patients. Blood withdrawal will be performed at the day care and will extend their visit to 60minutes. Visits are combined with a standard of care visit.

There is no primary benefit for the patients participating.
Future patients may possible benefit from more accessible and possible efficient CAR T-cell therapy.

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

• 18 years and older
• Be able to read, understand and give informed consent
• Have MM and belong to 1 of the following subgroups:
Group 1A: MM patients, triple refractory
Group 2A: MM patients, treated with BsAbs, either on treatment or within 3 months after discontinuation
Group 1B: MM patients having received first line treatment only
Group 1C: Newly diagnosed MM patients
Group 2B: MM patients > 3 months after BsAbs treatment discontinuation

• For the full scale experiment: the haemoglobin level should be > 6.5 mmol/L, lower haemoglobin levels (5,0-6,5 mmol/L) are accepted when blood withdrawal is

combined with an already scheduled routine blood transfusion.

Exclusion criteria

• not being able to give informed consent
• A lymphocyte count of < 0.5 x 10^9/L
• Use of corticosteroids > 20 mg a day in the 7 days before blood withdrawal. The same counts for any other immunosuppressant drug
• Haemoglobin level < 5,0 mmol/L
• For the full scale experiment: any condition which may possibly interfere with the safety of extra blood withdrawal.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2024
Enrollment:	50
Type:	Anticipated

Ethics review

Approved WMO

Date:	29-03-2024
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	NL85893.018.23