Individualized dosing of fludarabine during innate allo SCT: A randomized phase II study (TARGET Study)

Published: 23-07-2018
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To address whether the individualized fludarabine conditioning reduces the incidence of severe viral infections at day 100 within the context of an αβTCR / CD19 depleted transplantation regimen.

Ethical review	Approved WMO
Status	Completed
Health condition type	Leukaemias
Study type	Interventional

Summary

ID

NL-OMON55832

Source
ToetsingOnline

Brief title
TARGET Study

Condition

- Leukaemias

Synonym
hematological malignancies; blood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W,Miltenyi Biotec GmbH

Intervention

Keyword: &alfa, &beta, Hematological malignancies, Individualized fludarabine dosing, TCR / CD19 depleted transplantation

Outcome measures

Primary outcome

Cumulative incidence of severe viral infections at day 100.

Secondary outcome

- Non relapse mortality (NRM) at day 100

- aGVHD grade II-IV at day 100

- Donor engraftment (chimerism > 95%) at day 100

- Overall survival at day 100

- Cumulative incidence of relapse at day 100

- Effective fludarabine exposure

- Cost effectiveness at 2 years

Study description

Background summary

Allogeneic stem cell transplantation (allo-SCT) is still the treatment of choice for many patients suffering from hematological malignancies, which can only occasionally be cured with conventional chemotherapy. Allo-SCT still associates with a high transplant related morbidity and mortality. Fludarabine (FLU) is part of many regimens utilized for conditioning. Recent analysis of a retrospective allo-SCT patient cohort has shown that high exposure of FLU results in an increased risk of viral infections and subsequent change of non-relapse mortality.
With *individualized dosing of FLU* (section C4) we aim to reduce the change of overexposure to FLU, which to diminish the change of infectious complications.

Study objective

To address whether the individualized fludarabine conditioning reduces the incidence of severe viral infections at day 100 within the context of an αβTCR / CD19 depleted transplantation regimen.

Study design

Prospective, multicenter, open label randomized, phase II study

Intervention

Patients will be randomized to either to standard dosing of fludarabine or individualized fludarabine dosing as part of a conditioning regimen, followed by an αβTCR / CD19 depleted transplantation.

Study burden and risks

The protocol comprises a different dosing of fludarabine in the experimental arm. All other acts, measurements, follow-up and level of care are therefore similar to off-study patients undergoing allo-SCT. The burden of the therapy is associated with the allo-SCT itself, which is a necessary therapeutic intervention in all subjects. Possible increased risks for the recipient are graft failures, although not observed so far in all cohorts with the intended dose levels. The intended target level of fludarabine remains in the range of all so far treated patients at the UMCU. We only propose to avoid too high exposure to fludarabine

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3508 GA
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3508 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Adults (>= 18 years)
2. AML, MDS, ALL, CML, CLL, NHL, HL, or a myeloproliferative disease (MPD)
3. Indication for allo-SCT according to the policy of the local center
4. WHO performance status <= 2
5. Written informed consent

Exclusion criteria

1. Relapse of disease within 5 months after previous allo-SCT
2. Bilirubin and/or transaminases > 2.5 x normal value*
3. Creatinine clearance < 40 ml/min
4. Cardiac dysfunction as defined by:
- Unstable angina or unstable cardiac arrhythmias
- NYHA classification > II (Appendix B)
- Cardiac symptoms and/or history of cardiac disease AND a cardiac ejection fraction <45%
5. Active, uncontrolled infection

Study design

Design

Study phase:	2
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-03-2019
Enrollment:	98
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fludara
Generic name:	Fludarabin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-07-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	19-11-2018
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-10-2020

Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-02-2022
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 24753
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2018-000356-18-NL
CCMO	NL64877.041.18
OMON	NL-OMON24753