A prospective outcome study on patients with profound combined immunodeficiency

Published: 23-12-2016
Last updated: 17-04-2024

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON45905

Source
ToetsingOnline

Brief title
pCID

Condition

- Immunodeficiency syndromes

Synonym
immune deficiency; immune disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,vergoeding door studiecoordinator voor dataregistratie per geincludeerde patient

Intervention

Keyword: Immune deficiency, prosspective, quality of life, stem cell transplantation

Outcome measures

Primary outcome

The primary endpoint is overall survival determined after year 5. The event analysed is death from any cause. The time to this event is the time from the first major infection or major manifestation of immune dysregulation (documented retrospectively at the time of study entry) to death.

Secondary outcome

The secondary endpoint is the time point of HSCT. The time to this event is the time from the first major infection or major manifestation of immune dysregulation to HSCT.

Tertiary endpoint is the frequency of major infections or major manifestations of immune dysregulation during the observation period.

These endpoints will be used as prognostic factors in combination with a set of potentially predictive biomarkers in survival models in order to establish a risk model for P-CID patients.

In addition, within this study, all patients undergoing HSCT will be analyzed with a second set of endpoints to evaluate of the outcome of SCT.

Primary endpoint is overall survival after 6 months and 1 year of follow up

Secondary endpoints are engraftment, immune reconstitution and

clinical outcome assessed at 6 and 12 months after HSCT.

Study description

Background summary

Combined immunodeficiencies (CID) are a heterogeneous group of inherited immune disorders with impaired T cell development and/or function manifesting through increased susceptibility to infections and/or immune dysregulation. They can be delineated from SCID by their manifestation beyond the first year of life. Profound CID (P-CID) is a potentially life-threatening form of CID, in which SCT is a relevant consideration at diagnosis.
The main hypothesis of this study is: P-CID patients undergoing early HSCT have a better 5-year survival than
patients who undergo late HSCT or are not transplanted.

Study objective

The primary objective of the study is to provide natural history data on patients with P-CID, irrespective of whether they undergo HSCT or not. The goals are to determine survival, the frequency of severe events and quality of life 5 years after study inclusion.

The secondary objective is to develop a risk model for P-CID patients. The model is developed from a set of clinical and laboratory parameters obtained at diagnosis, at study inclusion and yearly thereafter.

The tertiary objectives of this study are to determine the effects of donor, recipient and treatment factors on the outcome of HSCT. The goal is to determine the quality of engraftment and immunological reconstitution and to determine the effects of these parameters on clinical outcome.

Study design

Prospective international multicenter cohort study (observational study). Enrolled patients will be evaluated and treated according to local institutional protocols. They will receive comparable baseline and followup evaluations across all participating centres, irrespective of the therapeutic strategy at the individual site.
There will be 6 study visits (scheduled yearly) for all patients. Because of the variable history prior to study inclusion, a morbidity score is determined for each patient at study visit 1. For those patients

undergoing HSCT, an additional 6 months post-HSCT visit will be documented. The study visits will document immunological parameters, severe events including major infections and major manifestations of immune dysregulation, severe transplant-related events and quality of life.

Study burden and risks

There will be no risk associated with participation in this study.
There will probably be no direct benefit for the individual participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Clinical and immunological criteria determine inclusion irrespective of the genetic diagnosis.
T cell criteria (2 out of 4)
o Reduced T cell counts (CD4 : <700, if <2y ; <500, if 2-4y ; <300, if >4y ; CD8 : <350, if <2y ; <250, if 2-4y ; <150, if >4y)
o Reduced thymic function (CD45RA+CD62L+ or CD45RA+CD31+ of CD4+ <30% <2y, <25% 2-6y, <20% >6y)
o Impaired T cell proliferation (PHA response <30% of lower limit of normal)
o Elevated fraction of */* T cells (>15% of total CD3+ T cells)
AND Clinical criteria
* At least one major infection criteria (viral, bacterial, opportunistic)
OR
* At least one major immune dysregulation criteria (granulomas, lymphoproliferative disease, unexplained interstitial lung disease, inflammatory bowel disease, autoantibody mediated disease, vasculitis) OR
* At least one malignancy criteria (lymphoid malignancies and virally induced malignancies)
AND Age >< = 1yr and << = 16yr at study inclusion

Exclusion criteria

No written consent available No written informed consent of patient or parents in case of minors available or no assent of minor if applicable;* Patients with a clinical diagnosis of SCID or Omenn syndrome within the first year of life
* P-CID Patients for whom decision for HSCT is taken at age <1yr
* Patients with Wiskott-Aldrich syndrome and CD40 Ligand Deficiency, because disease-specific prognosis and treatment data are available
* Patients undergoing gene therapy or ADA enzyme replacement will be followed using the same parameters, but will not be included in the analysis

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	4
Type:	Anticipated

Ethics review

Approved WMO Date:	23-12-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	02-03-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
Other	DRKS00000497
CCMO	NL56821.058.16