Treatment of severe steroid-refractory acute GvHD with mesenchymal stromal cells.
A phase III randomized double-blind multi-center HOVON study.

Gepubliceerd: 28-10-2013 Laatst bijgewerkt: 18-08-2022

The hypothesis to be tested is that the outcome in arm B is better than in arm A.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27391

Bron
Nationaal Trial Register

Verkorte titel
HOVON 113 MSC

Aandoening

graft-versus-host disease, steroid-refractory

Ondersteuning

Primaire sponsor: HOVON Data Center
Overige ondersteuning: Koningin Wilhelmina Fonds (KWF), HOVON, LUMC

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Proportion of patients responding to treatment of acute GvHD grade II-IV (with gut and/or liver involvement) at day 29.

Toelichting onderzoek

Achtergrond van het onderzoek

Allogeneic stem cell transplantation (SCT) is the only curative option for many patients suffering from hematological malignancies. Although providing cure for many patients, SCT may be accompanied by severe treatment-related side-effects, including acute Graft-versus-Host Disease (GvHD). Acute GvHD is a major cause of SCT-related morbidity and mortality. First line treatment consists of usually protracted immunosuppressive therapy with high dose corticosteroids often in combination with calcineurin inhibitors. A variety of second line immunosuppressive agents has been investigated for patients failing on corticosteroids, but no optimal treatment has emerged. Steroid-refractory acute GvHD has a high mortality rate and surviving patients often develop chronic GvHD, which severely reduces quality of life. Therefore, there is an urgent need for new and better treatment modalities. Several studies have indicated that third-party mesenchymal stromal cells (MSC) might be an effective therapy for steroid-refractory GvHD. MSC play a role in the regulation of hematopoiesis but also have putative immunomodulatory properties. Pilot studies have yielded encouraging results suggesting that MSC treatment may induce responses in the majority of patients. We therefore propose a phase III prospective randomized double-blind multicenter study, comparing early treatment with MSC to placebo in patients with steroid-refractory acute GvHD.

The study will focus on:

i) improving the response rate to treatment with MSC,

ii) studying safety,

iii) assessing progression-free survival,

iv) assessing GvHD-free survival,

v) evaluating the possibility to reduce the time required for pharmacological immunosuppression,

vi) assessing the incidence of severe bacterial, viral and/or fungal infections,

vii) reducing the incidence and severity of chronic GvHD,

viii) evaluating the quality of life of patients receiving MSC compared with controls,

ix) developing a predictive score allowing the identification of patients with acute GvHD that will respond to MSC treatment.

Doel van het onderzoek

The hypothesis to be tested is that the outcome in arm B is better than in arm A.

Onderzoeksopzet

Clinical, laboratory and QoL evaluations:

• At entry,

• At day 8, 15, 22 and 29,

• Thereafter at 6 weeks and at 2, 3, 6, 12, 18 and 24 months

All patients will be followed until 10 years after randomization.

Onderzoeksproduct en/of interventie

Eligible patients will be randomized to either standardized second line treatment only, consisting of mycophenolate mofetil (MMF) in combination with a placebo for MSC infusion, or MMF in combination with MSC at a dose of 2 x106 MSC per kg bodyweight IV. The first gift of MSC or placebo will be administered the day following randomization. The second gift will be administered 7 days after the first gift.
In addition, all patients will continue systemic treatment with steroids and a calcineurin-inhibitor.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

•Grade II-IV acute GvHD with gut and/or liver involvement, confirmed by histology of involved tissues (in case of gut and liver involvement histology of either one of these tissues is considered sufficient);

• Non-responsive to treatment with steroids and a calcineurin-inhibitor defined as:

- progressive disease or mixed response after 5 days of consecutive systemic treatment with steroids at a dose of 2 mg/kg and a calcineurin-inhibitor at therapeutic trough levels.

- stage 4 GvHD of gut and/or liver and deterioration of clinical parameters (gut) or increase of serum total bilirubin levels in umol/L (liver) after 5 days of consecutive systemic treatment with steroids at a dose of 2 mg/kg and a calcineurin-inhibitor at therapeutic trough levels

- stable disease after 10 days of consecutive systemic treatment with steroids at a dose of 2 mg/kg and a calcineurin-inhibitor at therapeutic trough levels.

- progressive disease after initial partial response of maximal 1 grade after 10 days of consecutive systemic treatment with steroids at a dose of 2 mg/kg and a calcineurin-inhibitor at therapeutic trough levels.

• Any age;

• Lansky / Karnofsky score of ≥20;

• Signed informed consent by the patient and/or parent(s) or legal guardian(s).

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

• Use of prophylactic MMF, Myfortic or other systemic treatment for acute GvHD ≤ 6 days prior to development of acute GvHD grade II-IV with gut and/or liver involvement;

• Systemic treatment for acute GvHD other than steroids and a calcineurin inhibitor (budesonide is considered a local treatment);

• Previous treatment with MSC;

• Progressive or relapsing malignant disease in case of NHL, HL, CLL, MM, and ≥ 5% blasts in the bone marrow in case of AML, ALL, CML;

• Requiring ventilator or vasopressor support;
• Poor performance not expected to survive 14 days;

• Known seropositivity of HIV, Hepatitis B and C, HTLV;

• Known uncontrolled toxicity for DMSO;

• Known anaphylactic reaction to penicillin or streptomycin;

• Known pregnancy;

• Any psychological, familial, sociological and /or geographical condition potentially hampering compliance with the study protocol and follow-up schedule.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind

Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-11-2013
Aantal proefpersonen:	150
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	28-10-2013
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL4076
NTR-old	NTR4227
Ander register	2012-004915-30 / NL42497.000.12 : HOVON 113 MSC
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A