Anti-CD20 therapy for the treatment of chronic graft versus host disease.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27646

Source
NTR

Brief title
R'mabcGVHD

Health condition

30 patients with a steroid refractory cGVHD will be treated with anti-B-cell therapy

Sponsors and support

Primary sponsor: Roche Nederland B.V.
Source(s) of monetary or material Support: KWF "support grant voor clinical related projects" (UU 2006-2685)

Intervention

Outcome measures

Primary outcome

Proportion of complete and partial responses. A complete response will be defined as a complete resolution of clinical evidence of chronic GVHD. A partial response will be defined by an improvement in any of the affected organs.

Secondary outcome

Proportion of patients with a histological response.

Study description

Background summary

Allogeneic stem cell transplantation (allo-SCT) is the treatment of choice of many hematological malignancies, owing to the graft-versus-leukemia (GVL) effect from the allogeneic donor T cells. Unfortunately, the positive effect of GVL is counterbalanced by graft-versus-host disease (GVHD), a major complication following allo-SCT of which the resultant multi-organ damage and immune deficiency significantly impair overall survival after SCT. GVHD can be distinguished in an acute and a chronic form. Acute GVHD is a distinctive syndrome of dermatitis, hepatitis and enteritis, while the term chronic GVHD describes a more pleiotropic syndrome. 60-70% of all patients receiving an allo-SCT and surviving beyond day 100 develop chronic GVHD. In our own institute (UMC Utrecht), the incidence of chronic GVHD is 60%, while 44% of all patients develop extensive disease. The first line treatment of extensive chronic GVHD consists of steroids with or without the addition of cyclosporin, depending on the existence of a thrombocytopenia (<100 x 10exp9/L). However, 58% of all patients with extensive chronic GVHD is refractory to steroid treatment. Although the contribution of donor T cells to the development of both acute and chronic GVHD is beyond doubt, the role of B cells is much less well defined. However, two observations suggest that B cells do contribute to GVHD. In the first place, autoantibodies can be detected in 15-90% of chronic GVHD patients. Secondly, three small-scale clinical studies have demonstrated that in vivo depletion of B cells with the CD20-specific Ab rituximab resulted in amelioration of chronic GVHD symptoms in heavily pretreated steroid-refractory patients. Preliminary analysis of skin and liver biopsies taken during chronic GVHD revealed the deposition of IgG Ab on epithelial cells and the basal membrane. Together, these findings prompt us to better define the role for B cells in the development of chronic GVHD. This improved understanding will serve two purposes. In the first place, a better insight into the pathogenesis of chronic GVHD is essential to develop new treatment modalities. In addition, development of novel prognostic markers that can predict the occurence of chronic GVHD may result in a risk-adapted prevention strategy of GVHD.

Study objective

B cells contribute to the development of cGVHD.

Intervention

Treatment with Rituximab once a week, for 4 weeks.

Contacts

Public
University Medical Center Utrecht, Department of Hematology/H03.102, P.O. Box 85500

Ellen Meijer
Utrecht 3508 GA
The Netherlands
+31 (0)30 2507230
Scientific
University Medical Center Utrecht, Department of Hematology/H03.102, P.O. Box 85500

Ellen Meijer
Utrecht 3508 GA
The Netherlands
+31 (0)30 2507230

Eligibility criteria

Inclusion criteria

1. Age > 18 yr;
2. Steroid refractory chronic GVHD, including skin localization;
3. No other treatment apart from steroids and when applicable standard GVHD prevention.

Exclusion criteria

1. Relapse with a life expectancy of < 6 months;
3. Severe infections.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Masking:	Open (masking not used)

Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2006
Enrollment:	30
Type:	Anticipated

Ethics review

Positive opinion

Date:	16-06-2006
Application type:	First submission

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
NTR-new	NL648
NTR-old	NTR709
Other	: N/A
ISRCTN	ISRCTN43525354

Study results

Summary results
N/A