

## Paper

# Clinically demonstrable anti-autoimmunity mediated by allogeneic immune cells favorably affects outcome after stem cell transplantation in human autoimmune diseases

W Hinterberger<sup>1</sup>, M Hinterberger-Fischer<sup>1</sup> and A Marmont<sup>2</sup>

<sup>1</sup>2nd Department of Internal Medicine, Donauspital, and Ludwig Boltzmann Institute for Stem Cell Transplantation, Vienna, Austria; and <sup>2</sup>Division of Hematology and Stem Cell Transplantation, S Martino's Hospital, Genova, Italy

### Summary:

To determine the role of allogeneic, autologous and syngeneic hemopoietic stem cell transplantation (SCTx) as a treatment for severe autoimmune disease (AID) we performed a literature search employing Medline, Cancer Lit and abstract books for reports on transplants for blood disorders and a concomitant AID. All reviews, case reports and abstracts available between June 1977 and September 2001 were used and attempts made to update them by e-mail by the corresponding authors. Disease-free survival (DFS) after allogeneic SCTx for 23 patients with severe aplastic anemia was 78% at 16 years and survival in unmaintained remission of concomitant AID was 64% at 13 years. DFS after allogeneic SCTx for 24 patients with hematologic malignancies was 87% at 15 years and survival in unmaintained remission for concomitant AID was 70% at 11 years. DFS after autologous SCTx for 24 patients with hematologic malignancies was 48% at 6 years and survival in unmaintained remission for concomitant AID was 29% at 3 years. Among 30 patients given allogeneic SCTx 19 developed graft-versus-host disease (GVHD) and 11 did not. Upon clinically justified discontinuation of all immunosuppressive therapy, 3/11 patients without GVHD relapsed with their concomitant AID (freedom of AID-relapse 69% at 9 years), whereas none of 19 patients with GVHD did so (log rank:  $P = 0.0135$ ). Freedom of AID-relapse was superior after allo SCTx compared to autologous SCTx (89% at 18 years vs 38% at 5 years; log rank:  $P = 0.0002$ ). Our data suggest that a graft-versus-autoimmunity effect after allogeneic hemopoietic SCTx mediates elimination of autoimmunity.

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**Keywords:** hemopoietic stem cell transplantation; autoimmune disease; graft-versus-autoimmunity

Animal models of autoimmune diseases (AID) have been used to study hemato-lymphatic ablation followed by allogeneic hemopoietic stem cell transplantation (SCTx).<sup>1,2</sup> This approach relies on the assumption that an AID may result from a mono- or a polyclonal stem cell disorder.<sup>3</sup> Transfer of an AID by a hemopoietic SCTx (bone marrow, blood) and the prevention of hereditary and spontaneous AID by an allogeneic bone marrow transplant in experimental animals has been reviewed.<sup>1,4</sup> Successful treatment of fully developed AID in inbred mice strains by allogeneic bone marrow transplantation has also been observed.<sup>1,4</sup> Different immune cells (immunocompetent T/B cells or polyclonal stem cells) give rise to different AID,<sup>5</sup> which may require different transplant approaches. Concordance of human AID in monozygotic twins is rare<sup>6</sup> favoring the role of environmental factors and autoantigens.<sup>1</sup>

Concerning treatment strategies in severe human AID, myeloablative conditioning provides most intensive immunosuppression and a subsequent stem cell graft allows replacement or manipulation of hemopoietic stem cells. In allogeneic SCTx, a hypothetical graft-versus-AID activity has been postulated.<sup>7–9</sup>

In patients with AID, fibrotic lesions may be irreversible and responses after SCTx are difficult to assess. The role of SCTx in the treatment of severe AID, if there is one, has not yet been properly studied in controlled trials in humans.

We decided on an indirect approach to study responses of AID in humans after high-dose conditioning and a SCTx. We studied patients with aplastic anemia or a hematological malignancy who suffered from a concomitant AID and who were treated with an allogeneic SCTx. Autologous SCTx were also analyzed in patients with malignancies and a concomitant AID. We attempted to detect any superiority of allogeneic or autologous transplants in the treatment of AID.

### Materials and methods

#### *Analysis of published case reports*

Searches were performed to collect peer reviewed reports of blood stem cell transplants performed between June 1977 and September 2001 in patients suffering from aplas-

Correspondence: Dr W Hinterberger, Second Department of Medicine, Ludwig Boltzmann Institute for Stem Cell Transplantation, Donauspital, Langobardenstraße 122, A-1220 Vienna, Austria.  
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tic anemia, hematologic malignancies and a concomitant AID. We employed the literature search programs MedLine, PubMed and CancerLit and we reviewed abstracts from ASCO, ASH and EBMT meetings using the following keywords: allogeneic/autologous/syngeneic bone marrow, blood stem cell transplantation, leukemia acute, chronic, lymphoma, Hodgkin's disease, aplastic anemia, solid tumors, cancer, autoimmune disease, ankylosing spondylarthritis Bechterew, autoimmune hemolytic anemia (AIHA), autoimmune thyroiditis (AIT) Hashimoto, Crohn's disease, dermatomyositis, eosinophilic fasciitis, Grave's disease, idiopathic thrombocytopenic purpura (ITP), insulin-dependent diabetes mellitus (IDDM), multiple sclerosis (MS), myasthenia gravis, panarteriitis nodosa, psoriasis, rheumatoid arthritis (RA), Sjögren syndrome, systemic sclerosis, systemic lupus erythematosus, vasculitis.

We updated case reports by e-mail requests which included information on long-term follow-up, immunosuppression and graft-versus-host disease. Twenty out of 25 authors responded. We employed the statistical program SPSS for life table analysis, Kaplan–Meier plot estimates and log rank test.

#### *Allogeneic SCTx for aplastic anemia and a concomitant autoimmune disease*

Twenty-three patients with SAA (30 years, range 8–52 years, 18 females) suffered from a concomitant AID (Table 1).<sup>10–22</sup> The AID preceded the onset of aplastic anemia by 0.2–25 (median 3) years. Prior treatment for AID included gold salts, antirheumatic or thyrostatic drugs in at least 10 patients. Antibiotics including chloramphenicol were given to at least four patients. Patients received bone marrow transplants from HLA identical siblings ( $n = 22$ )

or from the mother ( $n = 1$ ).<sup>16</sup> Pretransplant conditioning consisted of cyclophosphamide (200 mg/kg on 4 consecutive days) in all cases (Table 1). Four patients also received irradiation (total body:  $n = 2$ ;<sup>14,18</sup> total lymphoid:  $n = 2$ ).<sup>18,19</sup> Four other patients received additional antithymocyte globulin alone (ATG)<sup>15</sup> or anti-lymphocyte globulin (ALG) together with procarbazine.<sup>22</sup> Standard graft-versus-host prophylaxis was given to all patients post transplant and consisted of methotrexate and cyclosporine, alone, or in combination.

#### *Allogeneic SCTx for hematological malignancy and a concomitant autoimmune disease*

Twenty-four patients with a hematological malignancy (36 years, range 14–56 years, eight females) suffered from a concomitant AID (Table 1).<sup>13,16,23–34</sup> The AID were detected 0.5 to 33 (median 8) years before transplant. Twenty-three patients received bone marrow transplants, which were T cell-depleted in two cases.<sup>25,28</sup> One of them was successfully retransplanted without T cell depletion because of relapsing AML.<sup>25</sup> Two bone marrow donors were unrelated, but completely matched.<sup>23,30</sup> One patient was grafted with circulating blood stem cells.<sup>33</sup> The majority of patients ( $n = 23$ ) were prepared with supralethal conditioning protocols, such as 120 mg/kg cyclophosphamide together with 12–15 Gy TBI or 16 mg/kg busulfan. One patient received a non-myeloablative conditioning regimen consisting of busulfan (8 mg/kg), fludarabine and ATG (Table 1).<sup>33</sup> 'Others' refers to one protocol including total body and total lymphoid irradiation together with cyclophosphamide 120 mg/kg and etoposide<sup>28</sup> and another unspecified agent.

**Table 1** Patient diseases and concomitant AID treated with stem cells transplantation after conditioning

<i>Blood disorders given STx</i>	<i>n</i>	<i>Concomitant AID</i>	<i>Allo: SAA/Malig/Auto: Malig</i>
			<i>n</i>
Severe aplastic anemia	23	Rheumatoid arthritis	9/0/3
Malignancies (allo/auto)		Crohn's disease	0/8/4
CML	11/1	Psoriasis	2/6/4
AML	10/2	Systemic lupus erythematoses	2/0/4
ALL	1/3	Multiple sclerosis	0/3/3
Hodgkin's disease	2/2	Autoimmune thyroiditis (Grave's disease)	3/2/0
NHL	0/15	Autoimmune thyroiditis (Hashimoto)	2/0/0
CLL	0/1	Eosinophilic fasciitis	3/0/0
		Sjögren syndrome	0/0/2
Conditioning protocols		Insulin-dependent diabetes mellitus	1/1/0
SAA		Lupus discoides	1/0/0
Cyclophosphamide 200 mg/kg	15	Colitis ulcerosa	0/1/0
Cycloph + TBI/TLI	4	Dermatitis herpetiformis	0/1/0
Cycloph + ATG/ALG	4	Autoimmune hepatitis	0/1/0
Malignancy (allo/auto)		Vasculitis	0/1/0
Cycloph 120 mg/kg + TBI	14/2	Myasthenia gravis	0/0/1
Cycloph+ busulfan	7/4	Ankylosing spondylarthritis Bechterew	0/0/1
BEAM	0/9	Autoimmune hemolytic anemia	0/0/1
Other protocols	3/9	Hemophilia-A inhibitor	0/0/1

STx = stem cell transplantation; AID = autoimmune diseases; SAA = severe aplastic anemia; Malig. = malignancy; allo = allogeneic; auto = autologous; CML = chronic myeloid leukemia; AML = acute myeloid leukemia; ALL = acute lymphoblastic leukemia; NHL = non-Hodgkin's lymphoma; CLL = chronic lymphocytic leukemia; Cycloph = cyclophosphamide; TBI = total body irradiation; TLI = total lymphoid irradiation; ATG = antithymocyte globulin; ALG = antilymphocyte globulin; BEAM = carmustine, etoposide, cytarabine, melphalan.

#### Bone Marrow Transplantation

*Impact of graft-versus-host disease on remission status of autoimmune diseases after allogeneic SCTx*

Thirty patients with a blood disorder and a concomitant AID that was clinically active at the time of allogeneic transplant were included in this analysis. Immunosuppression was discontinued in these patients because of lack of GVHD and improvement in AID manifestations. Patients suffering from IDDM (Ref. 16, patient 4) and autoimmune hypothyroidism were excluded from the study due to incomplete antibody screening and to surgical or radioablative interventions (Ref. 16, patients 7, 8, 10). Also excluded were each one of two subjects with a durable 9-year remission of concomitant Crohn's disease prior to transplant (Ref. 23, patient 1 = Ref. 16, patient 13) and one with multiple sclerosis stable for 2 years after diagnosis and prior to transplant.<sup>34</sup>

*Syngeneic SCTx for hematological malignancy and concomitant autoimmune disease*

Two patients<sup>16</sup> suffering from chronic myelocytic leukemia and from T-lymphoblastic leukemia also suffered from IDDM or from autoimmune thyroiditis, respectively. Conditioning consisted of TBI (10 and 12 Gy, respectively) and cylophosphamide (120 mg/kg body weight).

*Autologous SCTx for leukemia or lymphoma and a concomitant AID*

Twenty-four patients (39.5 years, range 15–57, 13 females) with acute or chronic leukemia or lymphoma suffered from a concomitant AID (Table 1) (Refs 34–51, and Masszi, personal communication). The AID preceded the onset of the malignancies in all but one case, for 12 years (median, range 0.7–22). Conditioning protocols included TBI with 12 Gy in two patients and established high-dose chemotherapy protocols for the other patients (Table 1). Fifteen patients received peripheral blood stem cells; two of them were CD34<sup>+</sup> positively selected. Nine patients received bone marrow, two of them CD34<sup>+</sup> positively selected.

*Remission status of autoimmune disease after allogeneic vs autologous SCTx*

The allogeneic and autologous cohorts consisted of 30 and 23 graft recipients, respectively. One autologous recipient was excluded because of refractoriness of the AID.<sup>51</sup> Recipients dying from infection (one allogeneic) or from relapse (five autologous) were censored at death if AID was in remission ( $n = 6$ ).

*Subgroups of autoimmune diseases*

To further evaluate the impact of pathophysiology on responses to transplant, the AID were subgrouped into predominantly antibody mediated ( $n = 16$ ) (SLE, Grave's disease, AIHA, myasthenia gravis, vasculitis, hemophilia-A inhibitor) and predominantly cell-mediated diseases ( $n = 55$ ) (RA, MS, AIT Hashimoto, IDDM, psoriasis, Crohn's disease, colitis ulcerosa, autoimmune hepatitis, dermatitis

herpetiformis, ankylosing spondylarthritis Bechterew, eosinophilic fasciitis, Sjögren syndrome).

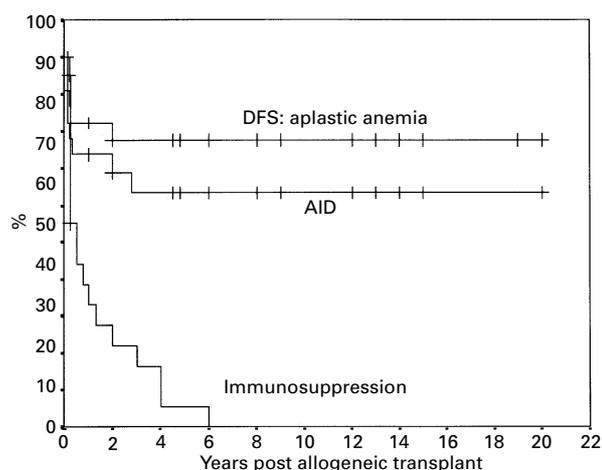
**Results**

*Outcome of aplastic anemia and concomitant autoimmune diseases following allogeneic SCTx (Figure 1)*

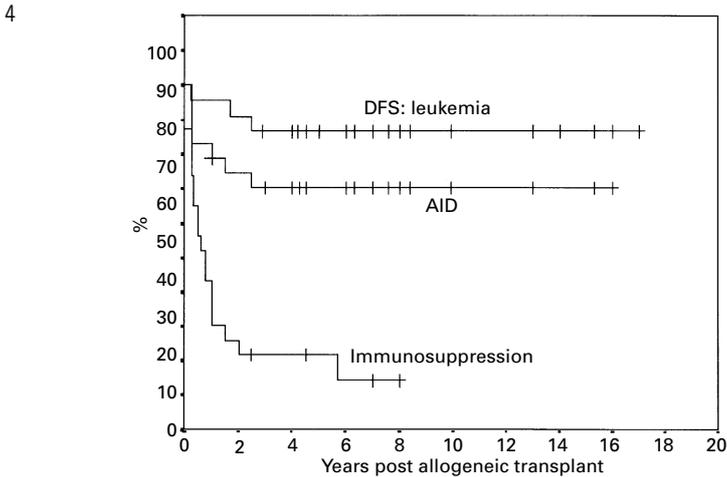
DFS was 78% at 16 years and survival in unmaintained remission of concomitant AID was 64% at 13 years. Five patients died from repeated marrow graft rejection, interstitial pneumonia, acute GVHD complicated by interstitial pneumonia or infection 75 days (median, range: 58 days–2 years) after transplant.<sup>10,18</sup> Nineteen patients surviving more than 100 days post SCTx received immunosuppressive therapy for graft-versus-host prophylaxis and for established GVHD for a total length of 6 months (median, range: 2–72). The concomitant AID failed to respond in two patients (IDDM (Ref. 16: patient 4), autoimmune thyroiditis (Grave's disease) (Ref. 16, patient 7)) but responded in 17 other patients.<sup>10–22</sup> One of these responding patients relapsed 32 months post transplant with rheumatoid arthritis,<sup>14</sup> while remaining in remission from aplastic anemia. Fifteen patients enjoy complete, unmaintained responses of their AID for 9 years (median, range: 1 to 20).

*Outcome of hematologic malignancies and concomitant autoimmune diseases after allogeneic SCTx (Figure 2)*

DFS was 87% at 15 years and survival in unmaintained remission of concomitant AID was 70% at 11 years. One patient with CML relapsed after 20 months from leukemia and died,<sup>23</sup> and two patients died 3 and 30 months after transplant in hematological remission from septic shock<sup>23</sup> and from sepsis related to immunosuppression for extensive GVHD.<sup>32</sup> GVHD prophylaxis and GVHD therapies were withdrawn after 6 months (median, range 2–72). Twenty-one patients experienced complete remission or pro-



**Figure 1** Disease-free survival (DFS), survival in unmaintained remission of a concomitant autoimmune disease (AID) and duration of immunosuppression (GVHD prophylaxis/therapy) in 23 patients after allogeneic stem cell transplantation for severe aplastic anemia (SAA).

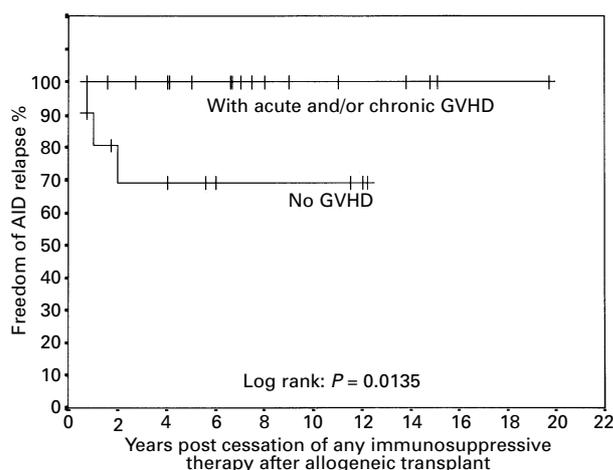


**Figure 2** Disease-free survival (DFS), survival in unmaintained remission of a concomitant autoimmune disease (AID) and duration of immunosuppression (GVHD prophylaxis/therapy) in 24 patients after allogeneic stem cell transplantation for leukemia.

gression-free survival of their AID for 7.3 years (median, range 1–17 years).<sup>16,24–31,33</sup> A case of Crohn's disease relapsed 18 months post graft, prior to leukemic relapse<sup>23</sup> and a case of psoriasis relapsed 12 months post transplant, while the malignancy remained in remission.<sup>13</sup>

#### *The impact of graft versus host disease on remission status of autoimmune diseases after allogeneic SCTx (Figure 3)*

Thirty out of 47 patients (17 with aplastic anemia) were evaluable for analysis. All of 19 patients exhibiting acute and/or chronic GVHD remained in unsupported remission of their AID for 6.6 years (median, range 0.75 to 19.7) upon discontinuation of immunosuppressive therapy. Three of 11 patients exhibiting no GVHD relapsed from their AID 0.7, 1 and 2 years after cessation of immunosuppression (follow-up 0.7–12.2 years, median: 5.8). Freedom of



**Figure 3** Freedom of relapse of concomitant autoimmune disease (AID) in 30 patients suffering from leukemia/lymphoma/aplastic anemia in relation to GVHD (graft-versus-host disease) manifestation post transplant. Immunosuppression discontinued (= day 0).

relapse was 69% at 9 years. This difference is significant (log rank test:  $P = 0.0135$ ). Complete donor type chimerism was reported in two of the AID cases who relapsed from AID.<sup>13,14</sup> The third patient (CML with concomitant Crohn's disease<sup>23</sup>) showed mixed chimerism on day 80, but no chimerism data were given at the time of AID (day 545) or CML relapse (day 680). Data on chimerism status of the eight non-relapsing no-GVHD patients are available only for two patients (both complete chimeras).

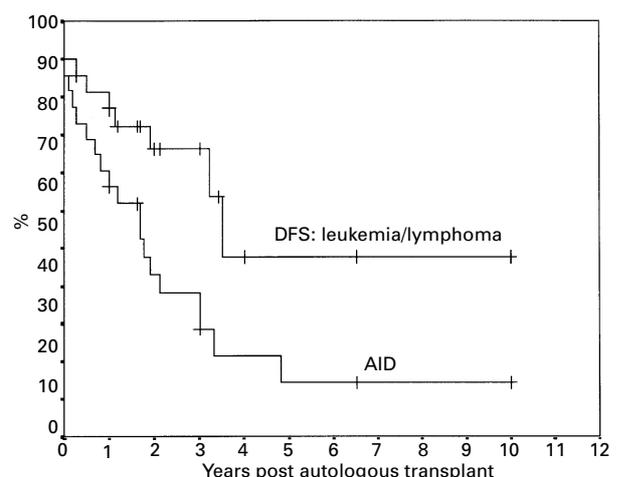
Two patients transplanted with syngeneic bone marrow grafts survived more than 14 years in remission.<sup>16</sup> A concomitant IDDM did not respond and a concomitant autoimmune thyroiditis requires permanent thyroid hormone replacement therapy.<sup>16</sup>

#### *Outcome of hematologic malignancies and responses of concomitant autoimmune diseases after autologous SCTx (Figure 4)*

DFS was 48% at 6 years and survival in unmaintained remission for concomitant AID was 29% at 3 years. There were seven relapses of the malignancies at 13 months post graft (median, 3–42).<sup>34,36,42,43,45,46</sup> Median survival in unmaintained remission of AID was 23 months (median, range: 3–120). Twenty-three of 24 patients experienced responses of their AID. The AID of 12 of these patients relapsed after 17 months (median, range: 1–36) (Refs 35, 37, 38, 40, 48, 50 and Masszi, personal communication). The AID of three out of four patients receiving CD34<sup>+</sup> positively selected bone marrow or peripheral stem cells relapsed after 20 months (median, range: 8–23).<sup>37,43</sup> Five patients died from relapsed malignancies the concomitant AID being in remission.<sup>34,42,45,46</sup> Five patients enjoy unmaintained remission of their AID for a median duration of 36 months (range: 19 to 120).<sup>41,44,47,49</sup>

A patient with large cell lymphoma and hemophilia A with a natural inhibitor of factor VIII experienced a reduction of factor VIII inhibitor from 752 to 1 BU/ml.<sup>39</sup>

Two of four patients with SLE relapsed after 12 and 36



**Figure 4** Disease free survival (DFS) and survival in unmaintained remission of a concomitant autoimmune disease (AID) after autologous hemopoietic stem cell transplantation of 24 patients with leukemia/lymphoma.

months post transplant.<sup>35,38</sup> One patient remained in unmaintained remission of SLE 78 months post transplant.<sup>41</sup> Another patient relapsed with CML and died 58 months post transplant while the SLE remained in remission.<sup>42</sup>

Four patients suffering from active Crohn's disease 8.5 years (median, range: 4–10) entered unsupported remission states of Crohn's disease for 1.5 years (median, range: 0.8 to 10 years) after transplant.<sup>44–47</sup> Two of them died from malignancy, while the Crohn's disease remained in remission for 10 and 25 months.<sup>45,46</sup>

Four patients suffering from psoriasis for 13, 15 and 20 years were given autologous transplants for comorbid hematologic malignancies. Complete remissions of psoriasis were obtained in four cases after transplant but relapses of psoriasis ensued 8, 20, 14 and 21 months post transplant, respectively (Ref. 37 and Masszi T, personal communication).

#### *Remission status of AID after allogeneic vs autologous SCTx*

Freedom of relapse from AID was 89% at 18 years after allogeneic SCTx and 38% at 5 years after autologous SCTx (log-rank:  $P = 0.0002$ ).

#### *Subgroups of autoimmune disease*

Antibody-mediated and cell-mediated subgroups of the AID did not differ with respect to responses to transplant (data not shown).

## Discussion

This study summarizes the courses of patients reported between June 1977 and September 2001 who were given bone marrow or blood stem cell transplants for blood disorders and concomitant autoimmune diseases (AID). Transplants utilizing donors suffering from an AID were also analyzed. A strong selection bias has most likely influenced publication of these cases and limits some of the conclusions drawn. Unexpected responses and successful outcomes after transplant were more likely subjects of detailed analysis and publication. Remission states of the blood disorders could reliably be drawn from the case descriptions whereas AID courses and responses to therapy were occasionally more difficult to judge. Clinical courses and responses to therapies were recently updated by contacting the respective authors in 20/25 cases. Response judgments of the reporting authors were generally employed. 'Cure' in systemic lupus erythematosus (SLE) is defined as a 'long-term and treatment-free clinical remission with restoration of normal blood counts and a normal immune system'. 'Possible cures' require an observation time of >10 years, and 'complete remissions' are defined as complete absence of symptoms and clinical signs of active lupus.<sup>52</sup> Corresponding criteria also apply for other severe AID. We elected the terms 'survival in unmaintained remission' and 'freedom of relapse' in this study to describe responses of AID. Another issue relevant for studying responses of AID

relates to the reversibility of lesions or to their irreversibility.

Cure of an AID may be anticipated upon replacement of self-reactive immunocompetent cells by healthy, non-self-reactive cells and no re-sensitization to persistent autoantigens.<sup>4,8,9</sup>

Allogeneic SCTx in our study proved highly effective in obviating the concomitant AID. Only five of 23 cases of concomitant AID failed to respond to the conditioning protocol given prior to an allogeneic SCTx. Three patients with Grave's disease pretreated by thyroidectomy or radioiodine and two patients with IDDM failed to respond. These disorders, obviously, remain poor targets for immune modulating therapies. Most  $\beta$ -islet cells are destroyed before detection of diabetes,<sup>53</sup> which makes the lesions irreversible. Three relapses of AID after initial responses to allogeneic transplants were documented. One patient each relapsed from rheumatoid arthritis,<sup>14</sup> psoriasis<sup>13</sup> and Crohn's disease.<sup>23</sup> Relapse of Crohn's disease was followed by leukemic relapse,<sup>23</sup> whereas two patients remained in remission with CML and SAA, respectively. These AID relapses were among 11 patients exhibiting no GVHD manifestation post transplant. No single relapse of an AID, however, was detected in 19 patients exhibiting GVHD manifestations after allogeneic transplantation. This difference provides evidence for a graft-versus-AID activity. A graft-versus-autoimmunity effect contributing to AID eradication has been hypothesized.<sup>4,7</sup>

Allogeneic SCTx, however, bears a higher risk of severe early complications. Early toxicities may soon become more manageable with non-myeloablative conditioning. Such conditioning has successfully been employed in animal models<sup>54,55</sup> supporting the concept of non-myeloablative conditioning before allogeneic SCTx in human AID too,<sup>7</sup> as already performed for malignant diseases.<sup>56</sup> However, reduced intensity regimens have not uniformly proved effective in human AID. A case of autoimmune thrombocytopenic purpura, refractory to splenectomy, was treated with reduced intensity conditioning and an allogeneic transplant from an HLA-identical sibling. Improvement in ITP ensued subsequent to the establishment of full donor chimerism after five donor lymphocyte infusions (own observation, AM).

Autologous stem cell transplantation has widely been proposed as a possible means of curing certain AID. Data presented in this study suggest significantly higher long-term unmaintained remission rates of concomitant AID after allogeneic as opposed to autologous transplantation. Conceivably, immunosuppression for GVHD prophylaxis and therapy may have attenuated AID courses post transplant. Nonetheless, these data show a much shorter duration of immunosuppressive therapy post transplant, as opposed to the duration of unmaintained remission of the AID (Figures 1 and 2).

The only relapses of AID in allogeneic graft recipients occurred in patients not exhibiting GVHD. If relapses of AID following allogeneic SCTx continue to be observed, the advantage of an allogeneic procedure over an autologous transplant would be weakened. Because of the selection bias and concomitant hemopoietic diseases, our data are not able to compare the long-term response rates of AID alone

after allogeneic or autologous SCTx. The impact of treatment-related mortality of the allogeneic procedure on survival probably may reduce its superiority.

We were unable to show any impact of purging stem cells from contaminating immune cells since three out of four patients receiving CD34<sup>+</sup> positively selected stem cells relapsed from AID. Identical twin transplants depict a clinical model of an autologous transplant without autoreactive T cells. They also depict an allogeneic model with a newly generated immune system devoid of GVHD prophylaxis and GVHD reactions. Hemopoietic stem cell transplants utilizing identical twin donors have only rarely been performed in proven or suspected AID.<sup>16,34,57,58</sup> Only two leukemic recipients exhibiting a concomitant AID (IDDM and autoimmune thyroiditis) received identical twin marrow grafts. The AID of these patients obviously had not been expected to respond. A patient with rheumatoid arthritis given an identical twin transplant obtained unmaintained remission for 2 years.<sup>57</sup> Although available data do not yet prove such a statement, identical twin stem cell grafts, if available, may turn out to be a preferable source of stem cell grafts for selected cases of AID. Aplastic anemia is a classical example of a serious disorder with an autoimmune pathogenesis in about two thirds of cases.<sup>58,59</sup> Replacement of the abnormal hemo-lymphatic system with normal or genetically modified stem cells may not only benefit patients with aplastic anemia, but also patients with other life-threatening AID. The therapeutic efficacy of SCTx in several serious disorders with an autoimmune pathogenesis is currently being explored. More than 350 autologous SCTx for AID alone have been collected by the EBMT (European Group for Blood and Marrow Transplantation) and by EULAR (European League Against Rheumatism). Prospective studies comparing autologous *vs* allogeneic transplants after high-dose therapy in cases of AID are currently lacking. Analysis of hemopoietic stem cell transplants in patients with serious blood disorders and a concomitant AID may help to characterize the autoimmune nature of certain diseases and may help to develop new treatment strategies.

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