EXTENDED REPORT

Haematopoietic stem cell transplantation for vasculitis including Behçet's disease and polychondritis: a retrospective analysis of patients recorded in the European Bone Marrow Transplantation and European League Against Rheumatism databases and a review of the literature

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Objective: To evaluate the feasibility of haematopoietic stem cell transplantation (HSCT) in vasculitis.
Methods: This is a retrospective analysis of patients who had received HSCT for vasculitic diseases and have been reported to the European League Against Rheumatism autoimmune disease or European Bone Marrow Transplantation ProMISe databases. Information about the disease and outcome was obtained by a questionnaire sent to the referring centres. Response of the disease to HSCT was defined as partial or complete responses according to the ability to reduce immunosuppression after HSCT. In addition, the Medline database was searched for reports on HSCT in patients with vasculitis.
Results: Detailed information was obtained for 15 patients, whose median age at HSCT was 37 years. The diagnoses were cryoglobulinaemia in four patients, Behçet's disease in three patients, Wegener's granulomatosis in three patients, and undifferentiated vasculitis, Churg–Strauss angiitis, polychondritis, Takayasu arteritis and polyarteritis nodosa in one patient each. 14 patients received autologous HSCT and 1 an allogeneic HSCT as the first transplant. In three patients, further transplantation was given because of relapse. The overall response, including all consecutive transplantations (HSCT/patient, n = 1–3, median 1.3) to HSCT, was 93%, with 46% complete responses and 46% partial responses; median (range) duration of response at the time of reporting was 45 (16–84) months. Three patients died, one from advanced disease, one from cancer and one from graft-versus-host disease. The Medline search showed five other patients who were effectively treated with HSCT for vasculitic diseases.
Conclusion: This retrospective study suggests that autologous HSCT is feasible for vasculitis. Its value remains to be tested in prospective controlled studies.

The systemic vasculitides are heterogeneous with respect to pathogenesis, manifestation and outcome. If untreated, the course is often fatal. Most patients with vasculitis respond to appropriate immunosuppressive treatment, the intensity of which depends on diagnosis and organ involvement. Intensive immunosuppression—for example, with cyclophosphamide—is the initial treatment of choice for necrotising small-vessel vasculitis with renal or lung involvement, for polyarteritis nodosa (PAN) and for other vasculitides, not improving with the standard treatment. Morbidity and mortality remain an issue of concern, with a five-year mortality for patients with necrotising vasculitis of about 20%, despite the availability of cyclophosphamide.[1] Moreover, the use of cyclophosphamide increases the risk of secondary malignancies such as myelodysplasia or secondary leukaemia, urinary bladder carcinoma and lymphoproliferative diseases.[2] Therefore, prolonged treatment with cyclophosphamide should be avoided. Case reports and uncontrolled small series suggest that rituximab (anti-CD20 antibody) may be effective in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis[3] and in cryoglobulinaemic vasculitis[4] in the short term. The tumour necrosis factor (TNF)α antagonist etanercept seems to be ineffective for Wegener's granulomatosis.[5]

Intensive immunosuppression with haematopoietic stem cell transplantation (HSCT) is an emerging alternative concept for patients with severe autoimmune diseases. Its aim is to alter the disease course through immunoablative treatment, followed by de novo T cell reconstitution.[6] Currently, up to 700 patients who have received a HSCT for severe autoimmune disease are registered in the European Bone Marrow Transplantation (EBMT) and European League Against Rheumatism (EULAR) databases. A detailed retrospective analysis of 473 patients showed a treatment-related mortality <10% and responses in 81% of patients,[7] most patients being severely affected by the autoimmune disease and not responding to standard treatment. Retrospective data for HSCT in systemic sclerosis, rheumatoid arthritis, systemic lupus erythematodes, juvenile rheumatoid arthritis, multiple sclerosis and autoimmune cytopenias have been published.[8] Randomised controlled studies are proceeding for different indications.

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; ATG, antithymocyte globulin; EBMT, European Bone Marrow Transplantation; EULAR, European League Against Rheumatism; G-CSF, granulocyte-colony-stimulating factor; GvHD, graft-versus-host disease; HLA, human leucocyte antigen; HSCT, haematopoietic stem cell transplantation; PAN, polyarteritis nodosa; TNF, tumour necrosis factor

Table 1 Patient's characteristics before autologous haematopoietic stem cell transplantation

Patient	Diagnosis	Age, sex	Organs involved, laboratory values, examinations	Treatment before HSCT	Months since diagnosis
1	Undifferentiated vasculitis	41, f	Kidney, active sediment, eye	Cyc, IV immunoglobulins	42
2	Behçet's disease	49, m	CNS involvement, fever, posterior uveitis	Cyc, steroids	84
3	Behçet's disease	32, m	Intracardial thrombus, pulmonalarterial aneurysma, polyarthritis	Cyc, MTX, steroids	63
4	Wegener's granulomatosis	46, f	Eye, nose, ANCA neg	Cyc	40
5	Wegener's granulomatosis	34, f	Lungs, sinus, kidney, c-ANCA 1:320	Cyc 100 g, CSA, kidney transplantation	132
6	Cryoglobulinaemia	42, f	Skin vasculitis with ulcers, arthritis, cryoglobulins 5.9 mg/ml	Chlorambucil	36
7	Cryoglobulinaemia	57, m	Arthritis, polyneuropathy	aPBSCT 2 years earlier, data lost	33
8	Cryoglobulinaemia	30, m	GN, severe pulmonary hypertension, sys pap >60 mm Hg	Plasmapheresis, Cyc 18 g	41
9	Churg–Strauss angiitis	31, f	Kidney, lung, LN, eosinophils 2200/μl, ANCA neg	Cyc 10 g, INF, CSA, AZA, MTX	84
10	Takayasu arteritis	22, f	Aortitis (PET), ESR 75 mm/h	Cyc 2 g, infliximab, anakinra, MTX	40
11	Polychondritis	36, f	Aortitis, scleritis, cartilages, ESR 100 mm/h	Infliximab, Cyc 13 g, fludarabine rapamycin, MMF	114
12	Polyarteritis nodosa	41, m	Skin, heart, brain, kidney, ESR 60 mm/h	Cyc >100 g	60

ANCA, antineutrophil cytoplasmic antibody; aPBSCT, autologous peripheral blood stem cell transplantation; AZA, azathioprine; c-ANCA, classical antineutrophil cytoplasmic antibody substitute circulating with classical; CNS, central nervous system; CSA, ciclosporin A; Cyc, cyclophosphamide; ESR, erythrocyte sedimentation rate; f, female; GN, glomerulonephritis; HSCT, haematopoietic stem cell transplantation; INF, interferon; IV, intravenous; LN, lymph nodes; m, male; MTX, methotrexate; neg, negative; PET, positron emission tomography; sys pap, systolic pulmonary arterial pressure.

However, detailed data for HSCT for vasculitic diseases have not been published so far. To evaluate the role of HSCT as a therapeutic option for patients with vasculitides, we performed a retrospective analysis of patients reported in the EBMT/EULAR databases.

METHODS

Study design

This is a retrospective analysis of patients reported to the EBMT data management ProMISe or the EULAR autoimmune disease database, and a review of the literature.

Patient selection

The EULAR autoimmune disease and the EBMT ProMISe databases were searched for patients transplanted for one of the following diagnoses: ANCA-associated vasculitis, PAN, giant cell arteritis, cryoglobulinaemia, Behçet's disease, Takayasu arteritis, polychondritis or undifferentiated vasculitis.

Data collection

To obtain detailed information on patients identified in the databases, we contacted the referring centres by mailing a questionnaire asking for the treatment regimen, diagnosis and course of disease. The questionnaire included laboratory parameters, autoantibody titre, urine analysis, organs involved in vasculitis, imaging results, medication, graft source, conditioning regimen, treatment-related morbidity and follow-up examinations. Referring physicians from the participating centres were requested to answer the questionnaire and to report all consecutive transplants. All protocols used in these patients had been approved by an ethics committee, in addition to written informed consent obtained from patients or the patients' parents before HSCT.

Definition of response to treatment

Response to treatment was defined according to the intensity of immunosuppression needed to control disease activity in each patient after HSCT. Referring physicians were asked to classify the disease response to treatment as follows: no change, partial response or complete response. Complete response means that the patient is off immunosuppressive treatment without disease activity, partial response means that after HSCT a substantial reduction of immunosuppressive treatment was possible. This nomenclature is used in other published retrospective trials.[7] The classification by the referring physicians was completed with the information on laboratory values and clinical parameters recorded in the questionnaire.

Literature search

A Medline search was performed to identify reports on patients who received HSCT for vasculitis not registered in the database.

RESULTS

The ProMISe and EULAR database search showed 24 patients matching the search criteria.

Only 7 of 16 treating centres answered the questionnaire. Information was available on eight patients from German centres, two from Italian centres and one patient each from Switzerland, England, Austria, France and Finland. No detailed information was available for nine patients from the remaining nine institutions. Diagnoses of these nine patients were cryoglobulinaemia in four patients, undifferentiated vasculitis in two, and PAN, Wegener's granulomatosis, Behçet's disease in one patient each. The 15 patients for whom more detailed information was obtained are presented.

Patients' characteristics

There were nine female and six male patients; mean (range) age at HSCT was 37 (10–57) years. Diagnoses were cryoglobulinaemia in four, Behçet's disease in three, Wegener's granulomatosis in three, and undifferentiated vasculitis, Churg–Strauss angiitis, Takayasu arteritis, polychondritis and PAN in one patient each. Tables 1 and 2 gives the patients' characteristics.

Treatment

All patients had active disease at the time of transplantation, having failed intensive immunosuppression, including cytostatic drugs. Pretransplant cumulative cyclophosphamide doses were given for six patients (table 1); two of them had received >100 g of cyclophosphamide before HSCT.

Fourteen patients received an autologous HSCT and one an allogeneic HSCT as the first transplant. In three patients, a further transplantation was given because of relapse: in one a further autologous, in one an allogeneic and in the third a further autologous followed by an allogeneic HSCT (table 2).

Table 2 Patients who received allogeneic transplantation: characteristics, treatment and outcome

Patient	Diagnosis	Age, sex	Organs involved	Treatment before Tx	Conditioning	ATG	Graft	TRC	Response	LFU (months)
13	Behçet's disease	30, f	CNS	AZA Cyc aPBSCT with BEAM/ATG relapse after 2 months	Cyc, thiotepa	–	Matched BM sibling	GvHD III degree liver	PR	+24
14	Wegener's granulomatosis	10, f	Kidney, lung, sinus p-ANCA 1:160	Cyc	Fludarabine, TBI	–	Matched BM sibling	GvHD I degree skin	CR p-ANCA neg	+60
15	Cryoglobulinaemia	57, m	Skin ulceration, mononeuritis multiplex	Cyc, plasmapheresis aPBSCT (Mel) (relapse after 2 years) 2. aPBSCT (Mel) with relapse	Cyc/Bu	+	Matched PBSC sibling	Death due to GVHD IV degree after DLI infusion	PR	+24

ANCA, antineutrophil cytoplasmic antibody; aPBSCT, autologous peripheral blood stem cell transplantation; ATG, antithymocyte globulin; AZA, azathioprine; BEAM, carmustine/etoposide/cytosine-arabinoside/melphalan; BM, bone marrow; Bu, busulfane; Cyc, cyclophosphamide; CNS, central nervous system; CR, complete response; DLI, donor lymphocyte infusion; f, female; GvHD, graft-versus-host disease; LFU, last follow-up; m, male; Mel, melphalan; p-ANCA, perinuclear antineutrophil cytoplasmic antibody; PR, partial response; TBI, total body irradiation; TRC, treatment-related complication; Tx, transplantation.

Stem cell mobilisation

The mobilisation regimen was cyclophosphamide 4 g/m^2, followed by granulocyte-colony-stimulating factor (G-CSF) 5 µg/kg body weight in nine patients, cyclophosphamide 6 g/m^2 and G-CSF 10 µg/kg body weight in three patients, cyclophosphamide 4 g/m^2 and 3 g/m^2 in two patients (patients 7 and 12, respectively). G-CSF was not used in patients7 and 12, because of the possibility of disease exacerbation after G-CSF application.

Conditioning regimen for patients who received autologous transplantation

The conditioning regimen for the 14 patients receiving autologous HSCT was: cyclophosphamide 200 mg/kg body weight and antithymocyte globulin (ATG) 80 mg/kg body weight for six patients, three of whom had a CD34 selected graft; 200 mg/kg body weight cyclophosphamide with a CD34 selected graft for one patient; 150 mg/kg body weight cyclophosphamide for another (patient 4; reduced dose was chosen because of mobilisation difficulties); melphalan 200 mg/m^2 with CD34 selection in three patients; melphalan 200 mg/m^2 in two; and cyclophosphamide 3 g/m^2 and melphalan 200 mg/m^2 in one patient. One patient received carmustine/etoposide/cytosine-arabinoside/melphalan (an analogue of the carmustine/etoposide/cytosine-arabinoside/melphalan protocol for Hodgkin's disease) with ATG (table 3).

Conditioning regimen and stem cell source for patients who received allogeneic transplantation

Three patients received an allograft from a related donor. Among them, one received human leucocyte antigen (HLA)-matched allogeneic bone marrow from a sibling, conditioning being fludarabine 90 mg/m^2 with total-body irradiation with 2 Gy and total lymph-node irradiation with 5 Gy. Another patient received allogeneic HLA-matched bone marrow transplantation from his brother because of progressive disease after autologous HSCT. In this case, the conditioning regimen was thiotepa 10 mg/kg body weight and cyclophosphamide 100 mg/kg body weight. A third patient received allogeneic HL-matched HSCT after undergoing two autologous HSCTs because of relapsing disease. Conditioning consisted of fludarabine, busulfane and ATG (table 2).

Response to treatment

At the time of this analysis with a median (range) follow-up for all patients of 44 (16–84) months, 12 of 15 patients who received transplantation were still alive. One patient died from advanced disease, one from graft-versus-host disease (GvHD) after donor lymphocyte infusion, and one from lung cancer. Seven patients achieved a sustained complete remission. Seven patients responded partially; low-dose maintenance immunosuppression was reinstituted for minor disease activity (patient data shown in tables 2 and 3). One patient showed stable disease (patient 8 in table 3). Overall response, including all consecutive transplantations (HSCT/patient, n = 1–3, median 1.3) was 92%, with 46% complete responses and 46% partial responses; median (range) duration of response at the time of reporting was 45 (16–84) months.

The response rate of the 14 patients who first received an autologous transplant was 86% (50% complete response, 36% partial response), with two relapses, 2 and 24 months after HSCT (patients 13 and 15). Patient 13 received allogeneic HSCT because of relapse after autologous HSCT, and 2 years after allogeneic HSCT he experienced a relapse with cerebral (headache) and oral (aphtous disease) manifestations. He was successfully treated with four, weekly cycles of rituximab 375 mg/m^2 with 1 g cyclophosphamide.[9] Patient 15 underwent a second autologous HSCT because of relapsing cryoglobulinaemic vasculitis

Table 3 Treatment and outcome of patients after autologous haematopoietic stem cell transplantation

Patient	Diagnosis	Mobilisation	Conditioning	Purging CD34	ATG	Graft	TRC	Response	LFU (months)
1	Undifferentiated. vasculitis	Cyc+G	Mel	−	+	aPBSCT	None	CR sediment normal	+63
2	Behçet's disease	Cyc+G	Mel	−	+	aPBSCT	Fever	PR aphtous disease	+62
3	Behçet's disease	Cyc+G	Mel	−	+	aPBSCT	Fever	CR	+72
4	Wegener's granulomatosis	Cyc+G	Cyc	−	−	aPBSCT	Fever	PR on MTX	+72
5	Wegener's granulomatosis	Cyc+G	Cyc	+	+	aPBSCT	EBV reactivation	CR BVAS 0	+72
6	Cryoglobulinaemia	Cyc+G	Cyc, Mel	−	−	aPBSCT	Sepsis in neutropenia	PR on AZA/steroids Cryoglobulins: trace	+84
7	Cryoglobulinaemia	Cyc	Cyc	+	−	aPBSCT	None	PR on steroids	+48
8	Cryoglobulinaemia	Cyc+G	Cyc	+	−	aPBSCT	DIC, sepsis neutropenia	NC cryoglobulin normal	26 died
9	Churg–Strauss angiitis	Cyc+G	Cyc	−	+	aPBSCT	None	PR on CSA eosinophils normal	+17
10	Takayasu arteritis	Cyc+G	Cyc	+	+	aPBSCT	EBV, CMV cardiotoxicity	CR ESR normal MRI normal	+16
11	Polychondritis	Cyc+G	Cyc	+	+	aPBSCT	Fever	CR ESR normal	+18
12	Polyarteritis nodosa	Cyc	Mel	−	−	aPBSCT	None	CR urine sediment normal	24 died

aPBSCT, autologous peripheral blood stem cell transplantation; AZA, azathioprine; BVAS, Birmingham Vasculitis Activity Score; CMV, cytomegaly virus reactivation; CR, complete response; CSA, ciclosporin A; Cyc, cyclophosphamide; DIC, disseminated intravascular coagulation; EBV, Ebstein-Barr virus reactivation; ESR, erythrocyte sedimentation rate; G, granulocyte-colony-stimulating factor; LFU, last follow-up; Mel, melphalan; MRI, magnetic resonance imaging; MTX, methotrexate; TRC, treatment-related complication; NC, no change; PR, partial response.

24 months after the first HSCT. A second relapse, 4 months later, was then treated by an allogeneic HSCT leading to a partial response lasting for 24 months.

Toxicity

One patient (patient 12) died 2 years after autologous HSCT from lung cancer in complete response of the underlying PAN. Patient 15 (table 2) who had partial response to his cryoglobulinaemia relapsed 24 months after allogeneic HSCT and died from GvHD grade IV after donor lymphocyte transfusion for mixed chimerism and rising cryoglobulin titre. This patient had previously received two autologous transplantations, 55 and 4 months before allogeneic HSCT. Patient 8 (table 3) showed no response to HSCT and died 26 months after HSCT from right ventricular failure due to severe pre-existing pulmonary hypertension.

Neutropenic fever was reported in six patients, and cytomegaly virus and Epstein–Barr virus reactivation occurred in two patients (patients 5 and 10); both patients had ex vivo and in vivo T cell depletion with ATG and CD34 selection of the graft. Patient 5 had transient pancytopenia and fever due to active Epstein–Barr virus infection.[10] Disseminated intravascular coagulation was reported in one patient (patient 1), and transient cardiotoxicity (reversible electrocardiogram changes and chest pain without troponin elevation) in another (patient 10).

Flare-up of disease after administration of G-CSF for stem cell mobilisation was not reported. Tables 2 and 3 show the treatment and outcome of the patients who received allogeneic and autologous transplantation, respectively.

Results of the Medline database search

In the Medline database, data on 12 patients, including 7 patients from this study (patients 2, 3, 5, 9–11 and 13), [9–12] treated with HSCT for vasculitic disease have been published. The characteristics and outcome of the five patients not included in the EBMT or EULAR databases are as follows. One patient was transplanted with CD34-selected autologous peripheral blood stem cells for PAN. Conditioning consisted of fludarabine, CAMPATH (alemtuzumab) and cyclophosphamide. Stem cells were mobilised with cyclophosphamide and G-CSF. The patient showed a complete response 18 months after HSCT.[13] A 4-year-old child with intestinal Behçet's disease, resistant to prednisolone, azathioprine, ciclosporin, tacrolimus, methotrexate, cyclophosphamide and TNFα antagonists was reported on by Rossi *et al*.[14] Autologous stem cells were mobilised with cyclophosphamide, followed by G-CSF. Conditioning consisted of fludarabine, cyclophosphamide and ATG; CD34 selection of the graft product was performed. The patient is off medication 2 years after transplantation and without disease activity. Voltarelli *et al*[15] reported on a patient with Takayasu arteritis resistant to conventional treatment, including cyclophosphamide, TNFα antagonists, mycophenolate mofetil and chlorambucil, who achieved complete remission after autologous HSCT. Stem cells were mobilised with cyclophosphamide, followed by G-CSF. Conditioning in this case consisted of cyclophosphamide and ATG, with CD34 selection of the graft. The patient is off immunosuppressive treatment 1½ years after HSCT. One child underwent non-myeloablative, HLA-matched, allogeneic bone marrow transplantation for overlap syndrome and small-vessel vasculitis after failure of methotrexate and cyclophosphamide and development of severe iatrogenic Cushing's syndrome and liver toxicity.[16] Conditioning was performed with cyclophosphamide, fludarabine and total body irradiation. The child is now (36 months after transplantation) off medication without signs of disease activity. One patient with Wegener's granulomatosis received autologous CD34-selected HSCT for granulomatous eye disease. Stem cells were mobilised with cyclophosphamide, followed by G-CSF. For conditioning, cyclophosphamide was given. He is in complete remission 16 months after HSCT.[17]

DISCUSSION

This review of the EBMT and EULAR databases indicates that HSCT for vasculitis not responding to conventional treatment is feasible and may considerably alter the course of the disease. The high response rate to HSCT of these heavily pretreated patients is promising and the responses seem to be durable in most patients. Most centres used a conditioning regimen based on cyclophosphamide. Lymphocyte depletion was often used either ex vivo (CD 34 selection) or in vivo (ATG) or both. Cyclophosphamide in combination with ATG and/or CD34 selection of the graft is now the conditioning regimen in most phase III trials for autoimmune diseases (protocols are available at http://www.ebmt.org).

Autologous HSCT for vasculitis in this patient group was not associated with treatment-related mortality. The main side effects were transient and mostly associated with aplasia after

conditioning (neutropenic fever). One patient died from lung cancer 2 years after HSCT. The established risk factor was smoking; in addition, he had previously received a cumulative cyclophosphamide dose >100 g. It remains possible that HSCT-associated immunosuppression played an additional part in the development of malignancy. However, an increased incidence of secondary malignancies is reported in patients who had received a HSCT for malignant diseases.[18]

To our knowledge, two patients with a relapse of ANCA-associated vasculitis after G-CSF administration are described in the literature.[19] In this series, however, no exacerbation of ANCA-associated vasculitis after G-CSF administration for stem cell mobilisation was observed.

It is important to mention that the median age of patients with ANCA-associated vasculitis reported herein (37 years) was lower than that of patients reported previously in the literature.

Three patients received allotransplantation either primarily, or because of relapses after autologous HSCT; one of them died. Allogeneic HSCT in patients with autoimmune diseases has the potential to change genetically determined factors influencing ''autoimmunity'' through establishing a potentially ''non-autoimmune'' new donor-type immune system. This may be associated with a so-far poorly understood graft versus autoimmune effect. Long-term remissions in patients with autoimmune diseases after allogeneic HSCT are reported in case reports.[20] Further experience comes from patients with haematological malignancies and concomitant autoimmune diseases. Remission of Wegener's disease after allogeneic HSCT with reduced conditioning for leukaemia is reported.[21] Allogeneic HSCT with reduced intensity conditioning is therefore now discussed as treatment for severe autoimmune disease.[22] Concerns regarding toxicity through acute or chronic GvHD remain.

The effect of autologous HSCT on the immune system in patients with autoimmune diseases is not clear, and is possibly not only due to a more intense immunosuppression but also to a ''resetting'' of the autoaggressive immune response. In patients with multiple sclerosis, durable remissions were seen despite a full return of normal protective immunity.[23]

This report is limited by the heterogeneity of the data, the post hoc definition of response to HSCT, and the incomplete nature of data on 9 of 25 patients reported to the database. We lack uniformly accepted criteria that define ''response to treatment'' for each of the (rare) diseases that led to HSCT in this report. In the setting of this retrospective analysis, a relatively robust read-out for response to treatment is the intensity of post-HSCT immunosuppression needed to control each disease. This read-out is clearly limited and is influenced by the individual judgement of the physician.

Larger and prospectively designed clinical trials are thus needed to confirm these preliminary data. The key question remains the selection of patients for HSCT. The initial results with HSCT have shown that patients with reduced organ function and autoimmune disease have considerable treatment-related mortality.[24] In subsequent trials, therefore, those patients were excluded. The patients most likely to benefit from a more intense treatment must be identified as early as possible in the disease course. Established prognostic factors must be used to select patients at risk. For the group of necrotising vasculitidies, the Birmingham Vasculitis Activity Score and the five-factor score are correlated with long-term outcome and mortality.[25] Patients with renal, hepatic, cerebral and gastrointestinal involvement have a higher mortality in small-vessel vasculitides.[26] These risk factors should be considered for patient selection for HSCT.

We think that before proceeding to HSCT, standard treatment should be proved ineffective. This includes cyclophosphamide either orally or in monthly intravenous pulses. Owing to promising initial results and low toxicity, rituximab may also be considered before HSCT in patients with ANCA-associated vasculitis and cryoglobulinaemia.

In conclusion, patients with preserved organ function and poor prognostic factors failing to respond to cyclophosphamide should be considered for autologous HSCT. Owing to the limited number of patients treated so far, further experience with autologous HSCT for patients with vasculitis should be gained by developing a common international protocol. Such a protocol is in preparation.

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