lated from the beginning of salvage therapy, is 5 months (range 3-32).

In conclusion, this salvage regimen with high-dose ifosfamide and etoposide appears promising in patients with relapsed progressive NHL, and patient accrual will continue in this disease category. Both IFOVM and DHAP plus G-CSF allow adequate PBSC mobilization for one or two APBSCT procedures. In patients with refractory aggressive NHL the regimen appears to have little activity, and such patients should receive alternative experimental therapies.

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Transfusion requirement can be abolished by epoietin-α and autologous platelet predeposit in patients receiving high dose chemotherapy with stem cell support

In patients undergoing high dose sequential chemotherapy (HDS) for breast cancer (BC),[1] allogeneic platelet transfusions can be avoided by using cryopreserved autologous platelets.[2] Nevertheless, half of these patients develop a mild anemia before myeloblation, requiring eventually blood transfusion. In this cohort of patients, we evaluated the efficacy of recombinant human erythropoietin (EPO)[3,4] in preventing the development of anemia, and therefore any allogeneic transfusion requirement.

Sir,

Ten consecutive high risk BC patients undergoing HDS with PBSC transplantation entered the study. Relevant parient characteristics at baseline are reported in Table 1. HDS included high dose cyclophosphamide (HDCY, 7 g/m^2) plus G-CSF and, as the final myeloablative regimen requiring PBSC support ($\geq 5\times10^6$ CD34$^+$ cells/kg bw), melphalan (160 mg/m^2) and thiotepa (600 mg/m^2). Platelet transfusions were given when the platelet count dropped below 20×10^9/L or in the presence of bleeding episodes while red blood cell (RBC) units were transfused for Hb level < 8 g/dL. Epoietin-α (EPO-α) was administered at a dose of 10,000 U sc three times weekly plus oral iron supplementation starting after PBSC collection until myeloablation.

Autologous PCs were collected by a single plateletpheresis at platelet rebound after HDCY, when circulating platelet count exceeded 250×10^9/L. PCs were processed, stored and reinfused as previously described.[2] All patients completed the HDS program.

Before HDCY the median serum EPO concentration was 19.8 mU/mL, and in 5/9 patients the O/P ratio was < 0.8, revealing an inappropriate serum EPO concentration for the degree of anemia.[5] EPO-α was administered for 7 to 9 weeks, without any adverse effect. Changes in Hb level during EPO-α treatment and transfusion requirement are reported in Table 2.

Table 1. Baseline iron status and hematologic parameters of our 10 patients. Data are reported as mean ± SD (range).

Age, yrs (median, range)	43 (34-54)
Hb, g/dL	12.3±1.4 (10.1-14.5)
Serum iron, µg/dL	81±40 (11-132)
Transferrin saturation %	29±19 (2-59)
Serum ferritin, mg/dL	130±187 (16-594)
Serum EPO, mU/mL	13±6 (3.4-19)
O/P log EPO ratio	0.8±0.2 (0.3-1.0)

Table 2. Changes in Hb level during EPO-α treatment and transfusion requirement in the 10 patients studied.

Pts	Hemoglobin (g/dL)			Baseline O/P ratio	Transfusion requirement	
	Baseline	Before Epo	Before HDC		RBC (units)	PCs (single donor)
1	11.1	9.9	12.8	0.75	–	–
2	11.2	8.9	15.5	0.72	–	–
3	13.8	10.8	13.1	0.97	–	–
4	10.9	9.1	12.8	0.32	–	1
5	12.7	9.0	11.9	0.96	–	–
6	13.0	11.0	13.0	0.52	–	–
7	10.1	8.6	15.2	–	–	–
8	12.6	10.9	13.4	0.92	–	–
9	13.4	9.4	10.6	1.00	2	–
10	14.5	11.7	14.0	0.70	–	–
Mean±SD	12.3±1.4	9.9±1.1	13.2±1.4†	0.80	0.2*	0.1
Control M±SD (n=25)	12.7±1.0	–	10.9±1.0‡	0.79	0.8§	1.0

*†Hb level after vs. before EPO-α: p= 0.0003; ‡Hb level at baseline vs. before HDS: p <0.0001; *RBC requirement: study group vs. control: p = 0.033; §PC requirement: study group vs. control: p < 0.01.*

A single plateletpheresis allowing the collection and storage of an average 9.9×10^{11} platelets was performed in 9/10 patients. None of the patients receiving autologous PCs required allogeneic platelet support. After HDC and PBSC transplantation, one patient developed severe anemia (Hb < 8 g/dL) and required the transfusion of two units of RBC. Interestingly, this patient (#9) showed only a modest response to EPO-α. Due to gastric intolerance, she autonomously suspended iron intake and, although serum iron and ferritin remained within the normal range, a defective iron metabolism could not be excluded. The transfusion requirement of platelets and RBC was significanty lower ($p< 0.01$, and 0.033, respectively, see Table 2) in our study group than in 25 historical controls receiving HDS treatment and comparable amount of $CD34^+$ cells.

In conclusion, EPO-α given before HDC, along with the transfusion of autologous platelets, can substantially reduce the use of allogeneic blood products[6] in patients receiving a potentially curative intensified treatment. This novel approach can reduce the risks deriving from the exposure to allogeneic products and make the HDC approach possible in those patients who are unable to accept, e.g. for religious reasons, blood transfusions. On the other hand, 8 weeks EPO-α treatment (the average in our patients) is far more costly than 2 U of RBC ($1,800 and $310, respectively) which makes a cost-benefit analysis on a larger cohort of patients mandatory.

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