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Cost analysis and quality of life assessment comparing patients undergoing autologous peripheral blood stem cell transplantation or autologous bone marrow transplantation for refractory or relapsed non-Hodgkin's lymphoma or Hodgkin's disease: a prospective randomised trial

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Abstract

The cost-effectiveness of autologous peripheral blood stem cell transplantation (PBSCT) compared with autologous bone marrow transplantation (ABMT) for refractory or relapsed non-Hodgkin's lymphoma (NHL) or Morbus Hodgkin (MH) was assessed. Costs were determined from the induction chemotherapy regimen up to 3 months after discharge from hospital following the transplantation. Quality of life was measured by the EuroQol, the Rotterdam Symptom Checklist (RSCL) and the SF-36. Patients were randomised according to a 2:1 ratio to undergo either PBSCT or ABMT. 62 patients underwent PBSCT and 29 ABMT. Costs of the transplantation period were significantly lower in the PBSCT group (15 008 Euros) than in the ABMT group (19 000 Euros). Significant differences in quality of life were all in favour of PBSCT and emerged using the RSCL, both on 14 days after the transplantation and three months after discharge. We conclude that PBSCT is associated with lower costs and a better quality of life than ABMT for patients with refractory or relapsed NHL or MH.

Keywords: Hodgkin's disease; Non-Hodgkin's lymphoma; Recurrence; Haematopoietic stem cell transplantation; Bone marrow transplantation; Cost-benefit analysis; Costs and cost analysis; Quality of life; Adjuvant chemotherapy

1. Introduction

For patients with refractory or relapsed Morbus Hodgkin (MH) or non-Hodgkin's lymphoma (NHL) of intermediate or high-grade malignancy, intensive chemotherapy followed by autologous bone marrow transplantation (ABMT) has been the preferred treatment since Philip and colleagues [1] demonstrated its superiority over single intensive chemotherapy in patients with NHL [2]. A few years ago, haematopoietic growth factors (HGF) became available, allowing the collection of haematopoietic stem cells from the peripheral blood after chemotherapy and HGF administration. In their prospective randomised trial, Klumpp and colleagues [3] found that HGF administration in patients undergoing PBSCT with or without autologous bone marrow accelerated the rate of neutrophil engraftment, shortened the duration of hospitalisation, and reduced the number of days on non-prophylactic antibiotics. Due to these advantages, HGF mobilised PBSCT has now largely replaced ABMT [4,5]. In a prospective randomised trial, PBSCT was found to be superior to ABMT in patients with NHL or MH with regard to platelet recovery [6]. Patients randomised to PBSCT needed fewer red blood cell transfusions and spent less time in the hospital. As hospital days are

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often one of the main components of the total costs in economic evaluations and PBSCT avoids anaesthesia and operating room procedures, an economic advantage of PBSCT over ABMT may be expected. Such an advantage was indicated retrospectively in cost analyses by several authors [7–11] and confirmed prospectively by Hartmann and colleagues [12]. Only a relative small number of studies have so far addressed the cost-effectiveness of PBSCT [13], although it is a topic of considerable interest. As the increase in the incidence of NHL is sustained, stem cell transplantations continue to be a significant burden on healthcare resources [14]. To our knowledge, it has not yet been studied to what extent the quality of life of these patients shortly after transplantation is affected and, particularly, if any differences in the quality of life of patients having undergone either PBSCT or ABMT can be observed. Therefore, we performed a comprehensive cost-effectiveness analysis, including quality of life measurements, using data from a prospective multi-centre trial in which patients with refractory or relapsed NHL or MH were randomised to receive either ABMT or HGF mobilised autologous PBSCT after having undergone a three-cycle induction chemotherapy regimen followed by high-dose conditioning chemotherapy. The clinical findings of this study have been reported separately [15]. In this article, the results of the cost-effectiveness analysis are reported in detail.

2. Patients and methods

2.1. Study population

The study population comprised patients aged 18–65 years with intermediate or high-grade MH or NHL who relapsed after or were refractory to primary chemotherapy. This randomised phase III trial was performed in six centres in The Netherlands between 1994 and 1998 (five university hospitals and one cancer centre).

2.2. Study design

All patients underwent induction chemotherapy, consisting of a DHAP course and a VIM course, separated by a 3–4 week interval. DHAP consisted of cisplatin (100 mg/m^2) on day 1 by a 24-h continuous infusion, cytarabine (2 g/m^2) on day 2 by a 3-h infusion which was repeated after 12 h, and dexamethasone (40 mg orally or intravenously (i.v.)) administered daily on days 1–4. VIM consisted of etoposide (90 mg/m^2) i.v. on days 1, 3 and 5, ifosfamide (1200 mg/m^2) i.v. on days 1–5 and methotrexate (30 mg/m^2) i.v. on days 1 and 5. Patients who showed a partial ($>50\%$ tumour mass reduction) or complete response and a negative bone marrow biopsy after VIM were randomised according to a 2:1 ratio to undergo either PBSCT or ABMT. The remainder of the treatment consisted of another DHAP course and a high-dose conditioning chemotherapy regimen consisting of carmustine (300 mg/m^2) on day -6 (from graft reinfusion), etoposide (200 mg/m^2) and cytarabine (200 mg/m^2) on days -5 to -2, and melphalan (140 mg/m^2) on day -1 (the BEAM regimen). The graft was reinfused on day 0. In the PBSCT group, the harvesting of the stem cells had taken place by leucapheresis after the second DHAP course followed by granulocyte macrophage-colony stimulating factor (GM-CSF) treatment 5 μg/kg daily from the fourth day after the second DHAP course until the last leucapheresis (Leucomax®, Novartis, Basle, Switzerland). In the ABMT group, the bone marrow was harvested from the pelvis under general anaesthesia, prior to the second DHAP course (see Ref. [15] for an extensive description of the design).

2.3. Costs

In this analysis, the institutional perspective was taken [16]. The average total costs per patient were determined for the entire trial period, running from the start of the first DHAP course up to 3 months after hospital discharge after transplantation. The cost analysis was based on a database with all medical procedures, diagnostic tests, laboratory services, hospital days, daycare treatments and outpatient visits of all trial patients that were transplanted.

In contrast to charges, unit costs are the best estimators of the theoretically proper opportunity costs [16]. Therefore, we determined average unit costs for the most important cost items of our analysis (Table 1), reflecting real resource use, including a raise for overhead costs [17]. To determine the use of resources, we mainly followed the micro-costing method, which is based on a detailed inventory and measurement of all resources consumed [18]. The valuation of the resources and overhead costs was based on data from the financial departments of the two (university) hospitals with the highest number of patients in the trial (1997 level, 1 Euro = 2.20371 Dutch guilders). In each unit cost, a distinction to personnel costs (P), material costs (M) and overhead costs (O) was made. P included wages, social premiums and fees for irregular working hours of the haematologist, registrars, nursing staff and administrators. The haematologists and registrars were asked to estimate the time spent for each individual patient during a hospital day and an outpatient visit. Costs of nursing staff and administrators were calculated by dividing their total annual costs in the haematology department by the total annual number of hospital days. M comprised costs of disposables, equipment, regular nutrition (parenteral nutrition was calculated separately), laundry services and cleaning services. O contained bare hotel costs (without the already men-

Table 1
Unit costs (in Euros)

	Personnel	Materials	Overhead	Total
Haematology inpatient hospital day	160	53	113	326
Intensive care unit hospital day	530	166	252	948
Outpatient visit	52	4	20	76
Outpatient stay on daycare ward	29	40	79	148
Radiotherapy megavolt session	99	16	48	163
PBSCT				
Harvesting	366	417	196	979
Freezing	225	447	168	840
Defrosting	127	18	36	181
ABMT				
Harvesting	442	627	267	1336
Freezing	254	278	133	665
Defrosting	110	17	32	159

PBSCT, peripheral blood stem cell transplantation; ABMT, autologous bone marrow transplantation.

tioned laundry and cleaning costs) and the costs of non-medical departments of the hospital, like general management. The latter costs were not specifically known for the haematology department. Therefore, the total annual hospital costs on this item were determined, after which a part of these costs were allocated to the haematology department on the basis of the percentage square metres of the haematology department compared with the total amount of square metres of the entire hospital.

The unit costs are shown in Table 1. The unit cost of a haematology inpatient hospital day included costs for a possible stay in one of the isolation rooms of the haematology department. It also included costs of one 10-min visit (and 10 min of related work) of the haematologist during each hospital day. The latter is also included in the costs of an intensive care hospital day. An outpatient visit was assumed to take 15 minutes of the haematologist's time and an additional 15 min on work resulting from this visit. Costs of an outpatient stay on the daycare ward were particularly based on the resource use necessary for the administration of blood components. The costs of stem cell harvesting were based on an average number of two leucaphereses. The harvesting costs contain costs of 5.5 h of a research nurse's time and 1 h of the haematologist's time per leucapheresis. Material costs for bone marrow harvesting were higher than for stem cell harvesting as the former procedure was performed in the operating room. These fixed costs for stem cell transplantations and bone marrow transplantations were assumed to be the same for all patients who underwent PBSCT or ABMT, respectively.

For items with low costs or a neglectable influence (due to low average numbers), Dutch 1997 tariffs (of the Central Organ for Tariffs in Health Care, COTG) were used as approximations. Costs of medication were based on Dutch wholesale prices [19].

2.4. Quality of life

Economic evaluations require the use of a generic (non-disease-specific) instrument for health status measurement [20]. Therefore we used the EuroQol and the SF-36. In addition, the Rotterdam Symptom Checklist (RSCL) was applied as a cancer-specific questionnaire that is more sensitive to changes in health states of cancer patients. These instruments were included in written self-report questionnaires that were administered three times: the day before transplantation, 14 days post-transplantation and 3 months after discharge from the hospital. The SF-36 was not included in the second measurement, since the majority of questions in this questionnaire are not applicable to hospitalised patients.

The EuroQol questionnaire exists of two parts. The first part is a generic five-dimensional questionnaire, the EQ-5D. This profile can be transformed to a value given by the general public: the $EQ\text{-}5D_{index}$ [21]. The second part of the EuroQol questionnaire is a visual analogue scale, the EQ_{VAS}, which represents the patient's judgement of his own health state. The SF-36 measures functional status, well-being and general health perception on nine subscales which can be aggregated into two sum scores, physical health and mental health [22]. The RSCL mainly measures (cancer-specific) complaints and consists of 38 items, such as nausea and lack of energy [23]. Five items were added to measure complaints that were related to possible adverse effects of the treatment under study: painful joints, palpitations, rash, sweating and shivering.

2.5. Statistical analysis

The statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) for Windows, release 9.0.0. The Mann–Whitney test was used for the between-group comparisons of quality of life and cost

Table 2
Characteristics of the transplanted patients and main clinical findings [15]

	PBSCT ($n=62$)	ABMT ($n=29$)	P value
Mean age (median, range) (years)	49 (51; 18–64)	46 (50; 18–63)	0.32
Male/female (%)	68/32	48/52	0.11
NHL/MH (%)	85/15	72/28	0.16
Previous chemotherapy (%)	100	100	1.00
Previous radiotherapy (%)	32	35	1.00
LDH above 2× upper limit (%)	10	7	1.00
Time to neutrophil recovery (median days)	10	15	<0.01
Time to platelet recovery (median days)	13	18	<0.01
Red blood cell transfusions (median/patient)	6	10	0.02
Platelet transfusions (median/patient)	4	8	<0.02

NHL, Non-Hodgkin's lymphoma; MH, Morbus Hodgkin's; LDH, lactate dehydrogenase.

items, using a two-sided probability level of $\leqslant 0.05$. All data are presented as mean values.

3. Results

3.1. Patients

Characteristics of the 91 transplanted patients (62 PBSCT and 29 ABMT) and a summary of the clinical findings [15] are reported in Table 2.

3.2. Costs

The average total costs per patient of each distinct trial phase are presented in Fig. 1. Costs of the DHAP-VIM-DHAP induction chemotherapy preceding the transplantation were 11 182 Euros per patient on average (Table 3). Data on DHAP 1 costs were rarely available, as this course was primarily administered in referring hospitals. Costs of DHAP 1 + follow-up were therefore assumed to be equal to the costs of DHAP 2 + follow-up. Costs of the DHAP-VIM-DHAP regimen (including follow-up) were mainly determined by the costs of hospitalisation, as all courses were administered on an inpatient basis.

Costs of the harvesting phase (Table 3) were 4982 Euros in the PBSCT arm and 4741 Euros in the ABMT arm (non-significant (n.s.)). Patients undergoing PBSCT, as well as patients undergoing ABMT, were hospitalised for 4 days on average during this phase. In the PBSCT arm, two leucaphereses were necessary on average to obtain a useful graft. As the stem cells were mobilised by HGFs in the PBSCT arm, the related costs were significantly higher for these patients. They were nevertheless outweighed by the higher procedural costs in the ABMT arm, caused by the costs of anaesthesia and use of the operating room. Costs of blood components were also significantly higher in the ABMT arm.

The total costs of the follow-up after the harvesting phase (Table 3) did not differ significantly between both trial arms (PBSCT: 482 Euros; ABMT: 1598 Euros), although in the ABMT arm costs of hospital days, haematology outpatient visits, antibiotics and blood components were significantly higher.

The transplantation phase (Table 4) started with the high-dose conditioning BEAM chemotherapy regimen.

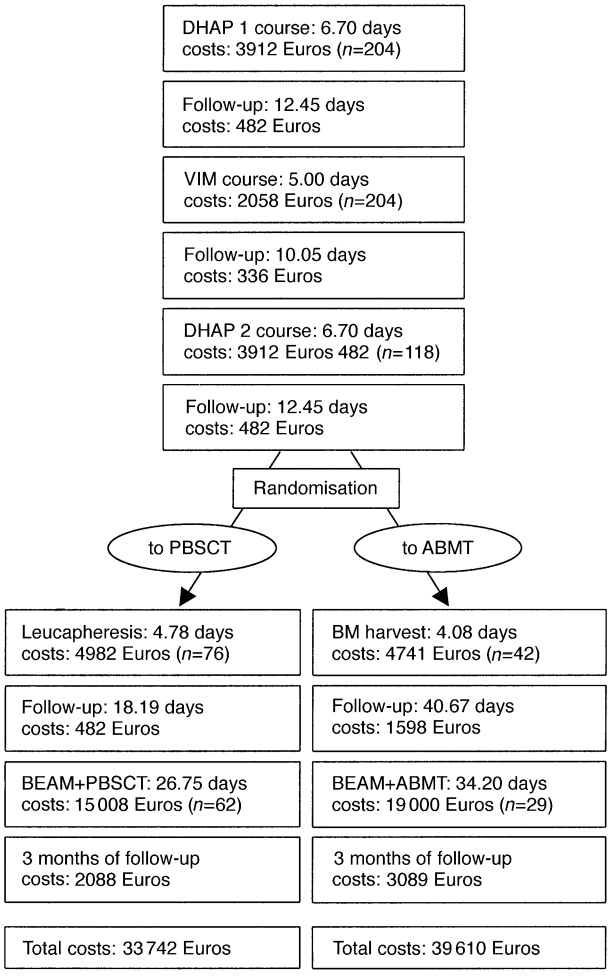

Fig. 1. Average costs per patient of the entire trial treatment, average number of days per phase. BM, bone marrow; ABMT, autologous bone marrow transplantation; PBSCT, peripheral blood stem cell transplantation.

Table 3
Average total costs per patient (in Euros) during the induction chemotherapy regimen, during the harvesting phase and during the follow-up after the harvesting phase

	DVD-ic	Harvesting phase			Follow-up after harvesting		
		PBSCT	ABMT	*P* value	PBSCT	ABMT	*P* value
Hospitalisation	6161	1468	1332	0.662	–	392	0.025
Daycare ward stay	134	25	–	0.307	8	98	0.026
Haematology outpatient visits	253	–	–	–	79	259	0.027
Consultations	35	4	25	0.026	122	55	0.125
Harvesting of transplant	–	979	1336	–[a]	–	–	–
Freezing of transplant	–	840	665	–[a]	–	–	–
Radiation therapy	158	–	–	–	–	–	–
Total parenteral nutrition	23	–	–	–	–	–	–
Blood components	904	376	663	0.003	1	312	0.007
Cytostatics	1413	–	–	1.000	–	6	0.116
HGF	289	830	–	0.002	–	68	0.116
Antibiotics	197	121	15	0.614	–	29	0.025
Other medication	337	41	232	0.189	–	14	0.025
Pathology diagnostics	28	–	48	0.000	3	–	0.524
Laboratory diagnostics	758	114	155	0.877	147	130	0.871
Microbiological diagnostics	21	21	9	0.657	2	7	0.138
Radiodiagnostics	400	39	74	0.190	58	96	0.120
Nuclear diagnostics	–	–	–	–	–	40	0.116
Other diagnostics	32	12	7	0.171	6	3	0.249
Other procedures	39	112	180	0.548	56	89	0.541
Total costs per patient	11 182	4982	4741	0.075	482	1598	0.271

DVD-ic, DHAP-VIM-DHAP induction chemotherapy regimen; HGF, haematopoietic growth factors; PBSCT, peripheral blood stem cell transplantation; ABMT, autologous bone marrow transplantation.
[a] Not compared, as these costs were assumed to be the same for each patient.

Table 4
Average total costs per patient (in Euros) during the transplantation phase (from high-dose conditioning BEAM chemotherapy regimen up to discharge from the hospital) and during the 3-month follow-up after the transplantation phase

	Transplantation phase			Follow-up after transplantation		
	PBSCT	ABMT	*P* value	PBSCT	ABMT	*P* value
Hospitalisation	9072	11232	0.0001	316	833	0.480
Daycare ward stay	–	–	–	221	290	0.372
Haematology outpatient visits	–	–	–	393	460	0.130
Consultations	108	124	0.714	52	39	0.867
Defrosting of transplant	181	159	–[a]	–	–	–
Radiation therapy	–	–	–	109	125	0.342
Total parenteral nutrition	243	321	0.222	3	1	0.755
Blood components	1680	2303	0.250	491	751	0.246
Cytostatics	809	710	0.012	–	–	–
HGF	13	53	0.059	–	–	–
Antibiotics	900	1575	0.038	8	1	0.750
Other medication	649	782	0.625	1	4	0.330
Pathology diagnostics	12	18	0.375	5	5	0.440
Laboratory diagnostics	752	904	0.039	197	282	0.187
Microbiological diagnostics	304	494	0.017	8	17	0.075
Radiodiagnostics	215	232	0.808	213	210	0.959
Nuclear diagnostics	16	5	0.779	46	49	0.919
Other diagnostics	30	81	0.052	8	2	0.235
Other procedures	24	7	0.335	17	20	0.701
Total costs per patient	15 008	19 000	0.0001	2088	3089	0.247

HGF, Haematopoietic growth factors; PBSCT, peripheral blood stem cell transplantation; ABMT, autologous bone marrow transplantation; BEAM, see text (Section 2.2).
[a] Not compared, as these costs were assumed to be the same for each patient.

In this phase, the PBSCT patients were hospitalised for a shorter time (26.75 days; range 8–51 days versus ABMT 34.20 days; range 24–78 days), which caused significantly lower hospitalisation costs during this phase (9072 Euro per patient; range 3263–20 434 Euros) compared with the ABMT arm (11 232 Euros; range 7830–27 346 Euros). Costs of antibiotics were also significantly lower in the PBSCT arm. Since hospital days were the main components of the total costs in the transplantation phase, the average total costs per patient were also significantly lower in the PBSCT arm (15 008 Euros; range 5284–31 761 Euros versus 19 000 Euros; range 10 937–47 408 Euros).

The average costs per patient of the 3-month follow-up period (Table 4) did not differ significantly between both study arms (PBSCT: 2088; range 95–11 735 Euros; ABMT: 3089 Euros; range 309–15 196 Euros). The main costs during this phase were the costs of the blood components and hospital days.

3.3. Quality of life

The main scores on the quality of life measurements are reported in Table 5. Regarding the generic EuroQol and the SF-36 measurements, there were no significant differences between both arms. On the RSCL, several items differed significantly. Fourteen days after the transplantation, ABMT patients reported more complaints concerning tiredness ($P=0.001$), lack of energy ($P=0.004$), headache ($P=0.025$), dizziness ($P=0.041$) and loss of hair ($P=0.012$). Of the items that were added to the RSCL to measure possible adverse effects of the treatment under study, palpitations ($P=0.049$), rash ($P=0.007$), sweating ($P=0.020$) and shivering ($P=0.002$) were reported more often in the ABMT arm. Three months after discharge from the hospital, ABMT patients reported more complaints about nausea ($P=0.023$), vomiting ($P=0.012$) and shivering ($P=0.011$).

Scores on the individual items of the RSCL can be summarised into three domain scores: physical complaints, mental complaints and an activity score. On the 14th day after transplantation, the physical complaints domain score was significantly worse in the ABMT arm (43.9 versus 34.5 in the PBSCT arm; $P=0.006$). The activity score, referring to the patient's functional status, was significantly better in the PBSCT arm on both the 14th day after transplantation measurement (48.4 versus 32.1 in the ABMT arm; $P=0.013$) as well as the 3 months after discharge measurement (68.9 versus 62.9 in the ABMT arm; $P=0.017$).

4. Discussion

In a prospective randomised multi-centre trial, we analysed the costs and effects of patients with refractory or relapsed non-Hodgkin's lymphoma (NHL) or Morbus Hodgkin's (MH) undergoing either autologous PBSCT or ABMT. Clinical results mainly comprised shorter times to neutrophil and platelet recovery, less red blood cell and platelet transfusions in the PBSCT patients [15]. These results confirm those found earlier in a prospective randomised trial of NHL or MH patients [6]. In the transplantation phase of our analysis, costs in the PBSCT arm were significantly lower compared with the ABMT arm. This was particularly caused by an earlier discharge of PBSCT patients (26.75 versus 34.20 days from start of the conditioning chemotherapy). In addition, costs of antibiotics were significantly lower in the PBSCT arm. The cost advantage of PBSCT has only been observed before prospectively by Hartmann and colleagues [12] in patients with solid tumours and lymphomas and confirmed by Smith and colleagues [9] who based their conclusions on the prospectively gathered data by Schmitz and colleagues [6]. Regarding quality of life, we found no significant post-transplantation differences using the generic EuroQol and the SF-36 questionnaires, implying that the overall health state of the patients is comparable among the PBSCT and ABMT groups. However, on the cancer-specific Rotterdam Symptom Checklist (RSCL), several differences were found in favour of PBSCT, indicating that NHL/MH patients undergoing PBSCT suffer less from those unpleasant cancer- and treatment-related symptoms than their counterparts undergoing ABMT.

An advantage of our study is its multi-centre design. As stated by Waters and colleagues [13], important cost differences between hospitals can occur in clinical practice, which are less likely to be expressed in the results, if the average total costs in a trial are based on data from several centres. Furthermore, our cost analysis is based on actual unit costs, which are generally considered to be the best estimators of opportunity costs [16]. However, only direct medical costs were assessed. Indirect costs (costs of lost production due to absence from work) were not calculated. In our opinion, the inclusion of these costs would not have undermined our main findings as no differences in quality of life between both study arms were found on the generic EuroQol and SF-36 questionnaires, which are indicative for the general health state of patients and the ability to work.

Our follow-up period was relatively short. Nevertheless, it contains an assessment of three months follow-up after discharge which has never been made before in prospective trials regarding costs of PBSCT versus ABMT treatment [14]. An indication for a slight (non-significant) cost advantage of PBSCT follow-up over the ABMT follow-up was found during these 3 months. The assessment of a longer follow-up period is unlikely to alter our main findings, since there is no evidence to indicate that follow-up costs after discharge

Table 5
Mean scores in both trial arms on EuroQol Visual Analogue Scale (EQ_{VAS}), EuroQol 5 Dimension Index ($EQ\text{-}5D_{index}$), SF-36 Physical Composite Score (SF-36 PCS), SF-36 Mental Composite Score (SF-36 MCS), SF-36 Physical functioning (SF-36 PF), SF-36 Role functioning—physical (SF-36 RP), SF-36 Bodily pain (SF-36 BP), SF-36 General health (SF-36 GH), SF-36 Vitality (SF-36 VT), SF-36 Social functioning (SF-36 SF), SF-36 Role functioning—emotional (SF-36 RE), SF-36 Mental health (SF-36 MH), Rotterdam Symptom Checklist (RSCL) Physical Symptom Distress Level (RSCL PSDL), RSCL Psychological Distress Level (RSCL PDL), RSCL Activity Level Impairment (RSCL ALI) and the six highest RSCL items scores (RSCL-i)[a]

Measurement	Day before transplantation		14 days after transplantation		3 months after hospital discharge	
	PBSCT	ABMT	PBSCT	ABMT	PBSCT	ABMT
EQ_{VAS}	68	66	55	50	73	70
$EQ\text{-}5D_{index}$	75	78	53	42	78	77
SF-36 PCS	40.1	39.2	–	–	40.8	38.1
SF-36 MCS	48.1	47.1	–	–	52.9	52.0
SF-36 PF	62.9	61.1	–	–	70.0	61.7
SF-36 RP	23.2	16.3	–	–	29.0	28.4
SF-36 BP	81.7	86.8	–	–	84.0	74.4
SF-36 GH	54.4	52.1	–	–	56.9	50.3
SF-36 VT	59.8	60.2	–	–	57.8	53.3
SF-36 SF	61.0	62.5	–	–	76.2	69.0
SF-36 RE	66.7	57.9	–	–	82.0	82.5
SF-36 MH	70.5	71.7	–	–	76.2	76.3
RSCL PSDL	20.1	22.9	34.5	43.9	15.7	21.2
RSCL PDL	19.4	24.0	22.3	20.8	17.5	23.0
RSCL ALI	63.2	59.8	48.4	32.1	68.9	62.9
RSCL–i (1st)	Loss of hair (2.43)	Loss of hair (2.78)	Lack of appetite (3.02)	Loss of hair (3.50)	Tiredness (2.59)	Tiredness (2.57)
RSCL–i (2nd)	Tiredness (2.21)	Tiredness (2.29)	Loss of hair (2.90)	Lack of appetite (3.41)	Sore muscles (1.90)	Dry mouth (2.22)
RSCL–i (3rd)	Difficulty concentrating (2.14)	Difficulty concentrating (2.21)	Sore mouth, pain when swallowing (2.75)	Sore mouth, pain when swallowing (3.32)	Worrying (1.85)	Sore muscles (2.13)
RSCL–i (4th)	Lack of energy (1.88)	Lack of appetite (2.00)	Nausea (2.58)	Tiredness (3.27)	Dry mouth (1.85)	Lack of energy (2.13)
RSCL–i (5th)	Worrying (1.85)	Worrying (2.00)	Tiredness (2.55)	Lack of energy (3.09)	Lack of energy (1.83)	Worrying (2.04)
RSCL–i (6th)	Difficulty sleeping (1.79)	Nausea (1.92)	Dry mouth (2.53)	Dry mouth (2.95)	Shortness of breath (1.71)	Difficulty concentrating (1.96)

PBSCT, peripheral blood stem cell transplantation; ABMT, autologous bone marrow transplantation.
[a] Ranges (worse to best) are 0–100 (EuroQol, SF-36, RSCL ALI), 100–0 (RSCL PSDL, RSCL PDL) and 4–1 (RSCL-i).

would reverse the results [12]. The similar post-transplant morbidity, mortality and overall survival between PBSCT and ABMT treatment arms in the Schmitz trial (median follow-up 311 days) supports this assumption [6]. Moreover, our findings are in agreement with a retrospective study [7] which showed lower follow-up costs for PBSCT than for ABMT during the first month after discharge.

Although our sample size was relatively small, it is the largest sample of NHL and MH patients considered up until now in a prospective randomised trial. Moreover, in the current sample, important differences were already found in both treatment costs and in the cancer-specific RSCL quality of life measurements. It can be argued that in a larger sample significant differences would have been found using the generic EuroQol and SF-36 quality of life questionnaires, which would have made the results even more convincing, as generic questionnaires are less sensitive for changes in health states than disease-specific questionnaires like the RSCL. An indication for such differences can be found in the results on the EuroQol $5D_{index}$, which was considerably, but not significantly higher in the PBSCT arm 14 days after transplantation.

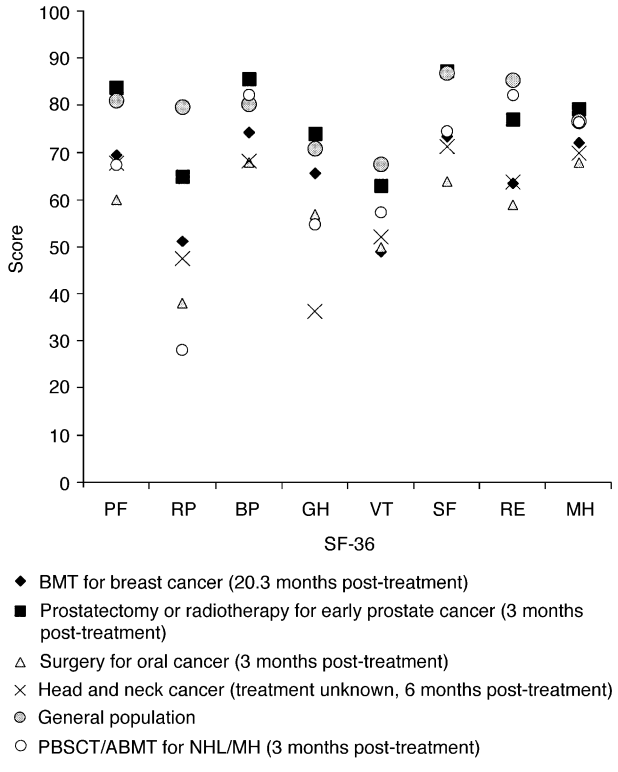

Fig. 2. Comparison of the mean SF-36 scores in the entire study group (PBSCT + ABMT, $n = 91$) to mean scores of the general Dutch population, which have been altered to resemble the age distribution of the study group [24]. Comparison to bone marrow transplantation (BMT) for breast cancer [25], to radical prostatectomy or radical external beam radiotherapy for early prostate cancer [26], to surgery for oral cancer [27] and to (unreported treatments in) head and neck cancer patients [28]. PF = Physical functioning, RP = Role functioning—physical, BP = Bodily pain, GH = General health, VT = Vitality, SF = Social functioning, RE = Role functioning—emotional, MH = Mental health. 0 (worst to 100 (best). PBSCT, peripheral blood stem cell transplantation; ABMT, autologous bone marrow transplantation; NHL, non-Hodgkin's lymphoma; MH, Morbus Hodgkin.

All cost-effectiveness analyses in PBSCT and ABMT trials so far have primarily used haematological outcomes as intermediate effect measures. Quality of life measurements have never before been made in the short term post-treatment comparison of patients having undergone either PBSCT or ABMT. The generic questionnaires used enable a comparison with other patient groups. For the SF-36 scores, we made such a comparison of the entire study group at 3 months after discharge to patients having undergone treatments for other neoplasms and to the general Dutch population with the same age distribution as our study group [24–28]. In this comparison (Fig. 2), our study group has not been divided into the PBSCT/ABMT arms as no significant differences between these groups had emerged in the SF-36 analysis. Although most scores for the PBSCT/ABMT-treated patients are in the range seen for the other cancer patients, the score on the physical role functioning scale is extremely bad. On the contrary, the score on the emotional role functioning scale is better than in any other group of cancer patients. Except for these differences, it seems that the quality of life of patients having undergone PBSCT or ABMT for NHL/MH is not very different from the quality of life of other cancer patients.

Regarding the cost analysis, absolute comparisons to earlier studies cannot be made due to the different methodologies and assumptions [13] and large variations in unit costs between countries [29]. For a comprehensive comparison of cost analyses in PBSCT/ABMT, we refer to Waters and colleagues [14]. Disregarding the absolute costs reported, a similarity in all prospective and retrospective studies focusing on differences in costs between PBSCT and ABMT for lymphomas is the observation of a cost advantage for PBSCT treatment over ABMT, ranging from 15 to 30% [8–12,30]. The relative cost advantage of PBSCT over ABMT in our analysis is 15%, or 21% if costs are considered from the harvesting phase onwards (as in most of the earlier studies).

To summarise, this study comprises the largest prospective randomised trial in patients with relapsed or refractory NHL/MH undergoing either PBSCT or ABMT treatment. The haematological outcomes are in accordance with earlier randomised clinical trials. Our study strongly confirms reports in the literature with a cost advantage for PBSCT treatment. In addition, it demonstrates a favourable quality of life for this arm of the study indicating that PBSCT is the treatment of choice for patients with refractory or relapsed NHL/MH.

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