A comparison of Cryopreserved and non-Cryopreserved Peripheral Blood Hematopoietic Stem Cells for Autologous Transplantation in Multiple Myeloma: A study from the Chronic Malignancies Working Party of the EBMT

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Abstract

Introduction

Most transplant centres cryopreserve peripheral blood stem cells (PBSC) for use in a subsequent autologous hematopoietic cell transplant (AHCT) using Dimethyl sulfoxide (DMSO) as a cryoprotectant. Non-cryopreserved (NCP) PBSC are used in autologous transplants for multiple myeloma (MM) in some countries with limited resources. We compared AHCT outcomes between patients in a large tertiary referral transplant centre in Oran, Algeria, who received non-cryopreserved PBSC and patients from EBMT-affiliated centres in countries where cryopreservation is standard.

Patients and Methods

MM patients who underwent AHCT between 2009 and 2020 inclusive using NCP PBSC were matched with up to four patients from 420 EBMT affiliated centres who received cryopreserved (CP) PBSC over the same period. Following standard procedures, PBSC were stored in a refrigerator at 4°C immediately following collection. PBSCs were then infused 24 hours following Melphalan administration (at a dose of either 140 or 200 mg/m^2). The primary endpoints were neutrophil and platelet engraftment as defined by standard EBMT

criteria. Secondary endpoints included non-relapse mortality (NRM), relapse incidence (RI), overall survival (OS) and progression free survival (PFS).

Results

Using NCP PBSC, 407 MM patients were autografted. The median number of collection procedures was two (range (r), (1-3)). The mean PBSC viability was 95% (r, 93.8-98.5%). 367 (90%) of these patients had at least one match with a patient in the EBMT registry who received CP PBSC. In total, 1,412 CP PBSC patients were included in this analysis. In the NCP group, the median dose of PBSCs collected was $3.2x10^6$ CD34+ cells/kg (interquartile range (IQR, 2.4-4.5); for the CP group (available in 12%), it was $4.0x10^6$ CD34+ cells/kg (IQR, 2.8-5.3) (p=0.005). The median number of days to neutrophil engraftment for the NCP and CP cohorts were 12 (IQR, 11 to 14) days, and 12 (IQR, 11 to 13) days, respectively (HR comparing CP versus NCP 1.13, 95% CI 0.99-1.29, p=0.08). Median time to platelet engraftment >20 x 10^9/L was similar in the NCP and CP cohorts: 12 (IQR, 11 to 14) days and 12 (IQR, 11 to 14) days, respectively. Non-relapse mortality rates at Day +100 were 0.3% (0.0-0.8%) and 0.7% (0.5-1.0%) respectively in the NCP and CP groups (p=0.38). The relapse incidence was lower in the NCP group (HR=0.23, p=0.004). The PFS up to 3 years was significantly longer in the non-cryopreserved cohort (HR=0.71, p<0.001). The OS rates at 3 years were 81% and 82% in the NCP group and the CP group, respectively (p=0.47).

Conclusion

This EBMT registry study, comparing the use of fresh cells at one center versus frozen cells from several centers, did not show a significant difference in terms of engraftment or NRM. These results allow us to conclude that the use of fresh cells can be an alternative to autografts for multiple myeloma in countries with limited resources.

Keywords:

Autologous; Peripheral blood stem cell; no-cryopreserved; multiple myeloma

Introduction

In multiple myeloma (MM), treatment intensification using high dose melphalan supported by autologous hematopoietic stem cell transplantation (AHCT) has been shown to improve response rates, progression-free survival and, in some trials, overall survival [1]. Almost all autologous transplants are currently performed using peripheral blood stem cells (PBSC) [2]. Globally, most transplant centres cryopreserve PBSC for use in a subsequent AHCT, using Dimethyl sulfoxide (DMSO) as a cryoprotectant [3]. This procedure requires expensive equipment and trained personnel. To avoid the high costs of establishing and maintaining a cryopreservation facility, some centres perform autografts without cryopreservation. Although non-cryopreserved short-term storage of hematopoietic stem cells is not standard practice, there have been several reports of autografts being performed safely without cryopreservation, the stem cells being stored in a conventional blood bank refrigerator at 4°C for up to four days [4-12]. We therefore compared AHCT outcomes between MM patients from a referral transplant centre in Algeria that uses non-cryopreserved (NCP) PBSC and patients from EBMT-affiliated centres in countries that traditionally use cryopreserved (CP) PBSC.

Methods

Patient selection

This was a retrospective, international, matched-pair analysis comparing patients from a tertiary referral transplant centre in Algeria who received NCP PBSC and patients from EBMT-affiliated centres in 23 countries where cryopreservation was standard. A total of 407 consecutive adult patients underwent a first MM AHCT in Oran, Algeria, between 2009 and 2020 inclusive.

Transplant procedure

PBSC collection was generally performed following five days of single agent G-CSF (10µg/kg). G-CSF was started on Tuesdays because the 'weekend' in Oran is on Thursdays and Fridays. If the patient required a second sample for another CD34+ count, it was done on the sixth working day. Stem cell collection was performed on either the Cobe Spectra® or Optia® using standard protocols. In the cohort of patients from Algeria, PBSC products were placed in the refrigerator for storage immediately following collection. Stem cell fridge storage time never exceeded 72 hours. The conditioning regimen was Melphalan at a dose of 200 mg/msq in the absence of renal impairment or 140 mg/msq in those with renal impairment. Melphalan was administered in a single dose in all patients. PBSC were infused over 30 minutes 24 hours following Melphalan administration. After thawing, PBSC viability was calculated using standard Trypan Blue and flow cytometric techniques.

Adult patients undergoing a first MM ASCT using cryopreserved PBSC during this time period were selected from the EBMT registry. The EBMT is a non-profit scientific society representing more than 600 transplant centres, most of which are in Europe. For this comparative analysis, we selected only centres in countries in which it is standard practice to cryopreserve PBSC in this setting. EBMT centres commit to obtaining informed consent according to the local regulations applicable at the time of collection and to report

pseudonymized data to the EBMT. The Chronic Malignancies Working Party of the EBMT approved this retrospective analysis. All patients in Oran gave their consent for this study.

A pair matched analysis

Patients receiving NCP PBSC in Oran were matched to a maximum of four patients from an overall cohort of 64,030 patients from 420 EBMT-affiliated centres in 23 countries transplanted between 2009 and 2020 inclusive. The countries and number of patients were as follows: Austria (26), Belgium (46), Bulgaria (6), Croatia (7), Cyprus (2), Czech Republic (46), Denmark (4), Estonia (5), Finland (5), France (231), Germany (213), Hungary (32), Ireland (13), Italy (194), Latvia (3), Netherlands (77), Poland (39), Portugal (17), Romania (15), Slovakia (2), Slovenia (8), Spain (93), Sweden (41) and United Kingdom (287).

Pair matching was based on the following criteria: (1) patient sex (M, F), (2) MM sub classification (IgG, IgA, light-chain only), (3) disease status at AHCT (CR, VGPR, PR, relapse/progression), (4) Melphalan conditioning dose (140 mg/sqm or 200 mg/sqm), (5) interval from diagnosis to AHCT, (6) date of AHCT, and (7) age at AHCT. Exact matching was used for the first four variables; nearest neighbor matching on the propensity score with a caliper width of 0.2 was used for the remaining three.

The primary endpoints were neutrophil and platelet engraftment as defined by standard EBMT criteria. Engraftment was calculated from the date of infusion of the stem cell transplant. Time to neutrophil engraftment was defined as the first of three consecutive days with a neutrophil count $>0.5\times10^9$/L and time to platelet engraftment the first of three consecutive days with an unsupported platelet count $>20\times10^9$/L. Secondary endpoints

included non-relapse mortality (NRM), relapse incidence (RI), progression-free survival (PFS) overall survival (OS).

Statistical analysis

Quantitative data were described by median and interquartile ranges (IQR). Qualitative data were presented by their frequency and proportion, calculated among subjects with no missing values for the corresponding variable. The median follow-up was calculated using the reverse Kaplan–Meier estimator. The cumulative incidence of neutrophil and platelet engraftment was estimated using the weighted crude cumulative incidence estimator with death as a competing event. Weights for the CP cohort were based on the number of matched CP patients to each NCP patient (weight equal to 1). Differences in time to engraftment between groups were assessed using cause-specific Cox proportional hazards regression models using exact ties and a robust variance estimator. Events were artificially censored after 28 days in the analysis of neutrophil recovery and after 100 days for platelet recovery. A hazard ratio above 1 indicates a shorter time to engraftment. The probability of OS and PFS was estimated using the weighted Kaplan-Meier method. Both the cumulative incidence of NRM and the cumulative RI were analysed in a competing event framework using the weighted crude cumulative incidence estimator. Differences between groups were assessed using (cause-specific) Cox proportional hazards regression models with a robust variance estimator and using Efron method of handling ties. All statistical tests were two-sided, and significance was determined when $p<0.05$. All analyses were performed in R version 4.2.2 using 'survival', 'cmprsk', 'prodlim' and 'MatchIt' packages.

Results

A total of 407 MM patients were transplanted using NCP PBSC.

Matching

There were 26 patients in the NCP cohort with missing data on one or more matching variables and 14 patients could not be matched to any of the 64,030 patients in the EBMT CP cohort. The patients who could not be matched were mostly younger patients who received reduced-dose Melphalan. In total, there were therefore 367 matched NCP PBSC patients. Most of these were matched to four CP PBSC patients (342 patients). For five NCP PBSC patients, only three CP PBSC patients were identified; for nine NCP PBSC patients, only two CP PBSC patients were identified and, finally, eleven NCP PBSC patients could only be matched to one CP PBSC patient. Therefore, the matched CP PBSC cohort was comprised of 1,412 patients (Figure 1).

Patients and disease characteristics

Patients and disease characteristics in both cohorts at diagnosis and at the time of transplantation are reported in Table 1. Regarding the clinical stage, a higher percentage of patients in the CP group had ISS stage I, 40.1% (n=274) *versus* 26.0% (n=54) in the NCP group, and a lower percentage of patients in the CP group had ISS stage III disease, 28.2% (n=193) *versus* 48.1% (n=100). The distribution of disease status at AHCT was similar in the two cohorts.

Induction

Data on induction regimens were only available in 13% of the matched EBMT CP PBSC patients though were available for all the Oran patients who received NCP PBSC. Several induction regimens were used (Table 2). Most patients with CP PBSC had one line of

induction therapy (74%); 25% had a second line of therapy prior to mobilization. In patients who received NCP PBSC, the corresponding percentages were 80% and 14%, respectively.

Mobilization

For the patients who received NCP PBSC, the median number of collection procedures was one (range, 1-3) and the median dose of PBSCs collected was 3.2 x 10^6 CD34+ cells/kg (range, 2.4-4.5). For patients who received CP PBSC (data available in 12%), it was 4.0 x 10^6 CD34+ cells/kg (range, 2.8-5.3) (p=0.005). In the patients who received NCP PBSC, the median graft storage time was 24 hours (range, 24h-72h) and the mean PBSC viability was 95% (range, 93.8-98.5%).

Conditioning regimen

The chemotherapy conditioning regimen was administered once a minimum of 2 x 10^6 CD34+cell/kg had been collected (Table 1).

Engraftment kinetics

The median durations of follow-up after AHCT in the NCP and CP cohorts were 66.6 (interquartile range (IQR), 41.3-96.1) and 45.3 (IQR, 13.6-79.6) months, respectively. Figure 2 shows the cumulative incidence of engraftment. The median times to neutrophil engraftment in the NCP and CP cohorts were 12 (IQR, 11 to 14) and 12 (IQR, 11 to 13) days, respectively, and the hazard ratio (HR) when comparing CP and NCP was 1.13 (95% CI 0.99-1.29, p=0.08). The median time to platelet engraftment >20 x 10^9/L was similar in the NCP and CP cohorts: 12 (IQR, 11 to 14) and 12 (IQR, 11 to 14) days, respectively. However, a lower percentage of patients achieved platelet engraftment within 100 days in the CP cohort (97%, 95% CI 96-98%) compared to the NCP cohort (100%). The cumulative incidence of

death before platelet engraftment was 0% in the non-cryopreserved cohort and 1.2% (95% CI 0.7-1.6%) in the cryopreserved cohort, which explains the better platelet engraftment in the NCP group. The hazard ratio (HR) of time-to-platelet-engraftment comparing CP versus NCP was 0.80 (95% CI 0.69-0.91, p=0.001).

All poor mobilizers, who collected fewer than 2 x 10^6 CD34+ cells/kg, were successfully autografted. Sixteen patients did not mobilize and were excluded from this study.

Non-relapse mortality, relapse incidence and survival

The cumulative incidence of NRM at Day +100 was 0.3% (95% CI 0.0-0.8) in the NCP PBSC cohort and 0.7% (0.5-1.0%) in the CP cohort (Figure 3a, HR 0.38, 95% CI 0.05-2.97, p=0.38). The cumulative RI was lower in the NCP cohort and was significantly different from that in the CP cohort (Figure 3b, HR 0.23, 95% CI 0.08-0.63, p=0.004). The difference in OS between cohorts was not significant (p=0.47). The OS at 3 years was 81% (95% CI 77-85%) and 82% (95% CI 80-85%) in the NCP cohort and the CP cohorts, respectively, Figure 3c. The PFS (Figure 3d) was significantly better in the NCP cohort; 3-year PFS was 58% (95% CI 53-63%) vs. 47% (95 CI 44-50%) in the CP cohort (HR 0.71, 95% CI 0.59-0.85, p<0.001).

Discussion

Autologous hematopoietic stem cell transplantation is the standard first-line treatment for multiple myeloma in eligible patients aged less than 70 years and with no or few comorbidities.

This technique, which use CP PBSCs, is very expensive and can be a barrier to its use, particularly in low-or middle-income countries with limited resources. The use of NCP PBSC may be an alternative to develop autograft in MM in these countries. The simplicity of this

technique on the one hand, the absence of toxic DMSO requiring washing of the graft, will also make it possible to reduce the costs of autograft.

The conditioning, which consists of a single intravenous infusion of Melphalan over 20 minutes at a dose of 200 mg/m^2 or 140 mg/m^2 in the event of renal impairment, is carried out in one day, which facilitates the conservation of the cell graft at +4°C in the refrigerator without altering the functionality of the PBSCs. Indeed, several studies have shown the possibility of storing PBSCs for several days (first five days) at +4°C without a major loss of their viability and thus MM becomes a preferred indication during autografts of fresh cells [13-14].

Comparison of the use of CP and NCP PBSCs during MM in our study with those of other centers showed similar engraftment results as well as the same NRM rates (Table 3) [15-22]. Furthermore, many centers have published their results of comparison between CP and NCP PBSCs during MM and have also shown similar results of engraftment and NRM, sometimes even the results are better during the use of NCP PBSCs as in, for example, Sarmiento et al, Bittencourt et al or Araujo et al (Table 4) [23-28].

In another context, particularly during allografts, the use of NCP PBSCs showed better results than with CP PBSCs in terms of engraftment (HR=0.82; 95% CI=0.69 to 0.97; p= 0.02) [29]. In a study of patients who underwent AHCT for Non-Hodgkin and Hodgkin Lymphoma using either CP or NCP cells, no significant differences in OS or PFS were reported (3-year OS: 85% vs 75%, p=0.3; PFS: 70% vs 61%, p=0.4) [30]. In our study, the method of stem cell storage was not associated with any difference in post-autograft OS. PFS, however, was better in the NCP cohort. This likely reflects differences in the use of maintenance treatment. The routine use of maintenance Thalidomide (100 mg/day every 21 days for 12 months) was introduced in Oran in 2009, whereas in Europe, maintenance treatment was only approved in

2017. Furthermore, it has been shown that post-autograft maintenance treatment in myeloma improves PFS [31]. Differences in the use of maintenance treatment between the NCP and CP cohorts may therefore have been a factor in the observed superior PFS in the CP cohort. Unfortunately, there was incomplete data on maintenance treatment in the CP EBMT cohort

Our study had the expected limitations of a retrospective analysis using data from different registries. We could not match patients based on ISS because of the high percentage of patients with missing data. Equally, Performance Score was collected using different measurement methods (ECOG and Karnofsky) so matching was also not possible. In those patients with available data, there was a higher percentage of patients with ISS III in the NCP cohort which may have resulted in estimates biased towards better OS and PFS for patients who received CP PBSC. There was also incomplete data on maintenance treatment in the CP EBMT cohort. In EBMT centres, no non-cryopreserved PBSC were used in the countries we selected.

The use of non-cryopreserved PBSC has one significant disadvantage in MM: The first is the impossibility of performing a tandem autograft in high-risk forms of MM. Secondarily,
it is not possible to store a portion of the graft for a second autologous transplant. However, the availability of novel therapies is likely to lead to reduced use of salvage transplants in myeloma over the coming years. In addition, for those patients with durable remissions who are considered candidates for a second salvage AHCT, it has been shown that stem cells can be successfully mobilised in this setting [32].

Furthermore, pharmacoeconomic studies relating to the evaluation in terms of costs of the collection, apheresis and preservation processes with a view to a second autograft, have

shown an overall additional cost of 2.5 million dollars, while only 1.4% of patients received a second autograft for catch-up and 90% of the grafts were unusable [33].

In addition, the use of a second salvage autograft during relapse is very uncommon, because,. new therapeutic classes such as monoclonal antibodies, T-cell engagers and CAR-T cells are increasingly available for the treatment of relapsed MM, reducing the likely future use of salvage transplants [34-35].

Conclusion

This EBMT registry study, comparing the use of NCP PBSCs at one center versus CP PBSCs from several centers, did not show a significant difference in terms of engraftment or NRM. These results allow us to conclude that the use of NCP PBSCs can be an alternative to autografts for multiple myeloma in countries with limited resources.

Disclosure of interest

The authors declare that they have no competing interest.

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Table 2: First induction regimen used in patients non-cryopreserved PBSC in Oran and in patients using cryopreserved PBSC in EBMT-affiliated centres (induction therapy data available in 100% in Oran and 13% in the EBMT).

	Non- cryopreserved		**Cryopreserved**	
	N	*%*	*N*	*%*
Total	367	100.0	187	100.0
VTD	146	39.8	61	32.6
VCD	97	26.4	19	10.2
VD	58	15.8	24	12.8
VAD	48	13.1	2	1.1
VRD	5	1.4	10	5.3
CTD	6	1.6	31	16.6
TD	2	0.5	6	3.2
PAD	2	0.5	6	3.2
Others	3	0.8	28	15.0

Non-cryopreserved and cryopreserved cohorts comparison using the $\chi 2$ test p-value <0.0001.
Foot notes : VTD= Bortezomib-Thalidomide-Dexamethasone; VCD= Bortezomib-Cyclophosphamide-Dexamethasone; VD= Bortezomib-Dexamethasone; VAD= Vincristine-Adriamycin- Dexamethasone; VRD= Bortezomib-Lenalidomide-Dexamethasone; CTD= Cyclophosphamide-Thalidomide-Dexamethasone; TD= Thalidomide-Dexamethasone; PAD= Bortezomib-Adriamycin-Dexamethasone.

Table 1: Demographic, disease and transplantation characteristics of patients receiving PBSCs stored at 4°C in Oran, Algeria and matched-pair patients receiving cryopreserved PBSCs included in the EBMT registry.

	Non-cryopreserved N (%)	**Cryopreserved N (%)**	**p-value**
Number of patients	367 (100)	1412 (100)	
Age at AHCT in years, median (IQR)	55.0 (49.2-60.0)	55.4 (49.3-60.2)	
<65	346 (94.3)	1327 (94.0)	0.41
65 or more	21 (5.7)	85 (6.0)	
Gender			
Male	220 (59.9)	843 (59.7)	0.98
Female	147 (40.1)	569 (40.3)	
MM sub classification			
IgG	218 (59.4)	843 (59.7)	
IgA	65 (16.8)	240 (17.0)	0.99
IgD	5 (1.4)	19 (1.3)	
Light-chain only	79 (21.5)	310 (22.0)	
Disease status at AHCT			
Complete response	107 (29.2)	422 (29.9)	
Very good partial response	179 (48.8)	673 (47.7)	0.98
Partial response	71 (19.3)	280 (19.8)	
Relapse/progression	10 (2.7)	37 (2.6)	
Interval diagnosis-AHCT in months, median (IQR)	7.9 (5.8-11.5)	7.1 (5.5-9.7)	0.35
Year of AHCT			
<2015	193 (52.6)	797 (49.4)	0.30
2015 or later	174 (47.4)	715 (50.6)	
Conditioning dosage			
Mel 140 mg/m^2	90 (23.3)	316 (21.3)	0.43
Mel 200 mg/m^2	296 (76.7)	1165 (78.7)	
ISS at diagnosis (missing in 43% and 52%, respectively)			<0.0001
I	54 (26.0)	274 (40.1)	
II	54 (26.0)	217 (31.7)	
III	100 (48.1)	193 (28.2)	

Non-cryopreserved and cryopreserved cohorts were compared using the $\chi 2$ test for categorical variables and the Kruskal-Wallis test for continuous data.

Foot notes: AHCT: autologous hematopoietic stem cell transplantation, MM: multiple myeloma, PBSC= peripheral Blood Hematopoietic Stem Cells, Mel: melphalan, ECOG: Eastern Cooperative Oncology Group, ISS=International Scoring System.

Table 3: Study results of engraftment with non-cryopreserved autologous peripheral blood progenitor cell transplantation.

Authors	Number of patients	Median CD34+ /10^6/kg	Median number of days to engraftment (95% CI): Neutrophils >0.5x10^9/L	Platelet>20x 10^9/L	NRM at day 100 (%)	N graft failure / N total
Ramzi (2012) [15]	38	3.6	11 (9-21)	13 (10-31)	0	0
Bekadja (2012) [16]	54	3.6	10 (6-17)	13 (9-24)	0	0
Kayal (2014) [17]	92	2.9	10 (8-27)	14 (9-38)	3.2	0
Bekadja (2017) [18]	240	5.7	10 (6-17)	13 (9-24)	1.3	0
Kulkarni (2018) [19]	224		12 (9-22)	17 (10-44)	3.1	1/224
Naithani (2018) [20]	59	3.6	11 (9-14)	11 (9-32)	1.7	0
Jennane (2020) [21]	55	4.5	12 (7-19)	14 (9-32)	3.6	0
Voloshin (2022) [22]	35	2.63	11 (9-14)	12 (8-19)	0	0

Table 4: Engraftment results and NRM in patients with cryopreserved and non-cryopreserved cells during autografts for multiple myeloma.

	Cryopreserved PBSC			Non-cryopreserved PBSC		P-value**	NRM%		
		Median number of days (IQR) to engraftment			Median number of days (IQR) to engraftment				
Study	n	NE	PE	N	NE	PE		*Cryo*	*No Cryo*	*P*
Sarmiento [23]	42	12	14 (12-18)	31	8 (8-11)	10 (10-19)	*<0.0001/ 0.0001*	0,5	0	0.9
Bittencourt [24]	63	13	NA	45	10	NA	*<0.0001*	5	2	NA
Piriyakhuntor [25]	16	10.5 (8-20)	12 (10-31)	26	12 (10-19)	14 (10-23)	0.20/0.89	0	0,7	0.61
Garifullin [26]	43	10 (8-14)	12 (8-20)	35	11 (9-14)	12 (8-19)	0.10/0.71	0	0	NA
Pessoa [27]*	51	98%	96.2%	54	90%	72.5%	*<0.01/<0.01*	NA	NA	NA
Araújo[28]	28	11.5	10.5	17	10	10.5	*0.045*	NA	NA	NA
This study	14 12	12 (11-13)	12 (11-14)	367	12 (11-14)	12 (11-14)	0.08/0.38	0.7	0.3	0.38

*Cumulative incidence at 25 days: 98% *versus* 90%, p<0.01 NE and 96.2% *versus* 72.5, p<0.01

** p-values for the comparison of NE/PE between patients with cryopreserved and non-cryopreserved PBSC

Foot note: NE= neutrophil engraftment; PE= platelet engraftment; NRM= non relapse mortality; NA=not available; PBSC=peripheral blood stem cells

Legends to figures

Figure 1:
Flow diagram of patient selection.

Figure 2:
Cumulative incidence of a) neutrophil and b) platelet engraftment after AHCT utilizing non-cryopreserved PBSC and matched AHCT utilizing cryopreserved PBSC.

Figure 3:
Cumulative incidence of a) non-relapse mortality (NRM), b) cumulative relapse incidence (RI), probability of overall survival (OS) and d) progression-free survival after AHCT (AHCT: autologous hematopoietic stem cell transplantation) in patients with non-cryopreserved peripheral blood stem cells (PBSC) and a matched cohort of patients with cryopreserved PBSC.

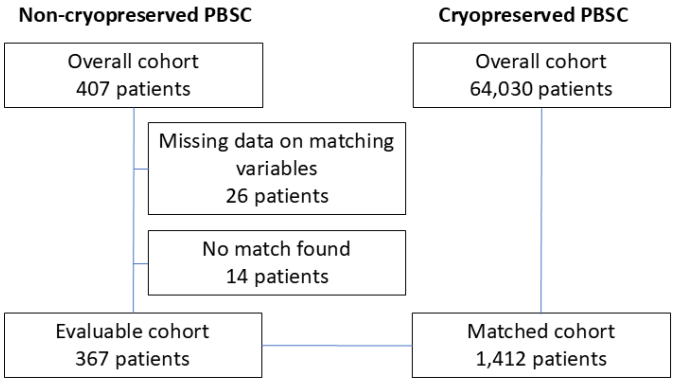

Non-cryopreserved PBSC
Cryopreserved PBSC
Overall cohort
407 patients
Overall cohort
64,030 patients
Missing data on matching variables
26 patients
No match found
14 patients
Evaluable cohort
367 patients
Matched cohort
1,412 patients

Figure 1:

Figure 2:

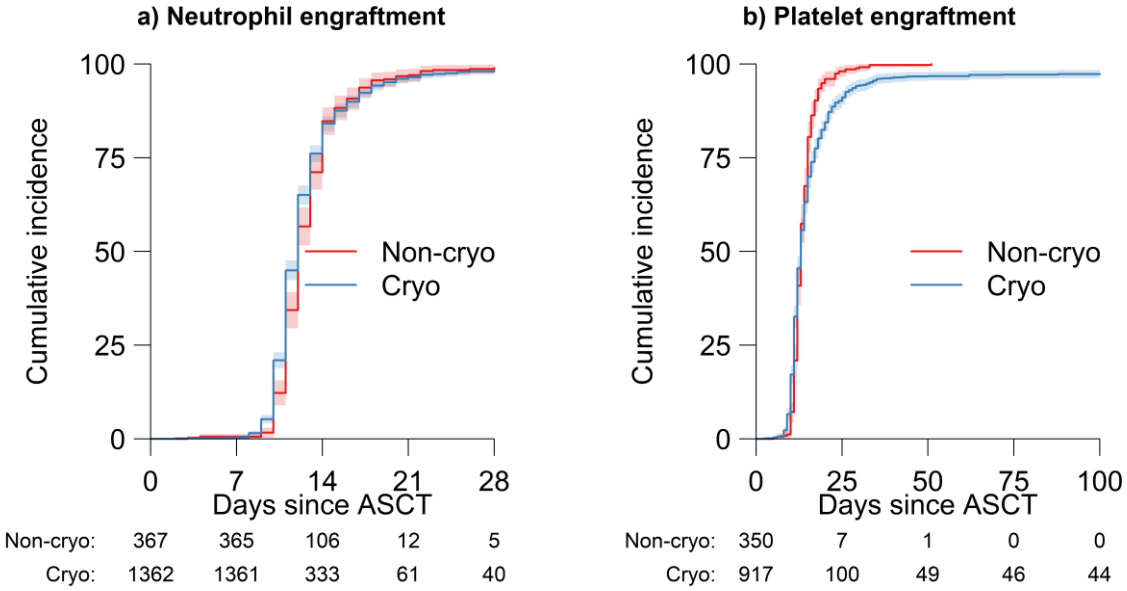
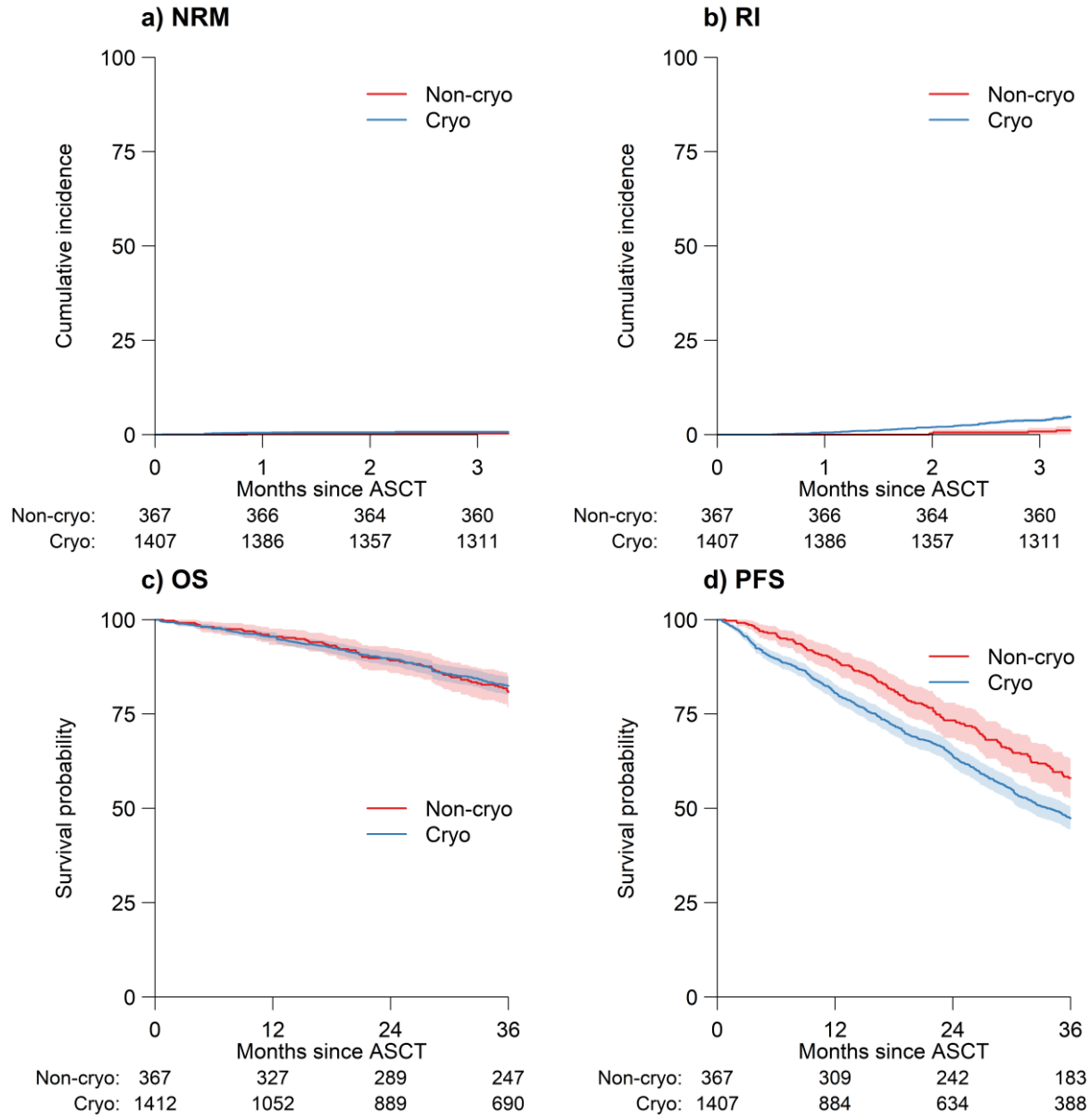

a) Neutrophil engraftment
Cumulative incidence
100
75
50
25
0
Non-cryo
Cryo
0
7
14
21
28
Days since ASCT
Non-cryo: 367 365 106 12 5
Cryo: 1362 1361 333 61 40
b) Platelet engraftment
Cumulative incidence
100
75
50
25
0
Non-cryo
Cryo
0
25
50
75
100
Days since ASCT
Non-cryo: 350 7 1 0 0
Cryo: 917 100 49 46 44

Figure 3:


a) NRM
Cumulative incidence
100
75
50
25
0
Non-cryo
Cryo
0
1
2
3
Months since ASCT
Non-cryo: 367 366 364 360
Cryo: 1407 1386 1357 1311
b) RI
Cumulative incidence
100
75
50
25
0
Non-cryo
Cryo
0
1
2
3
Months since ASCT
Non-cryo: 367 366 364 360
Cryo: 1407 1386 1357 1311
c) OS
Survival probability
100
75
50
25
0
Non-cryo
Cryo
0
12
24
36
Months since ASCT
Non-cryo: 367 327 289 247
Cryo: 1412 1052 889 690
d) PFS
Survival probability
100
75
50
25
0
Non-cryo
Cryo
0
12
24
36
Months since ASCT
Non-cryo: 367 309 242 183
Cryo: 1407 884 634 388