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## Costs of second allogeneic hematopoietic cell transplantation

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### Abstract

**Background**—A second allogeneic transplant following a prior allogeneic (allo-alo) or autologous (auto-alo) hematopoietic cell transplantation (HCT) is usually performed for graft failure, disease recurrence, secondary malignancy and as planned auto-alo transplant for some diseases.

**Methods**—We sought to describe the costs of second allogeneic HCT and evaluate their relationship with patient characteristics and post-transplant complications. Clinical information and medical costs for the first 100 days after transplantation of 245 patients (allo-alo: 55, auto-alo: 190) who underwent a second HCT between 2004 and 2010 were collected.

**Results**—Median costs of the second allogeneic HCT were \$151,000 (range \$62,000–405,000) for the allo-alo group and \$109,000 (range \$26,000–490,000) for the auto-alo. Median length of hospital stay was 23 days (range 0 - 76) for the allo-alo group and 9 days (range 0–96) for the auto-alo group. Only the year of transplant and post-transplant complications were significantly associated with costs in both groups when both pre- and post-transplant variables were considered. The overall costs of the second HCT were higher than the first in the allo-alo group. For the auto-alo group, there was no difference between the costs whether done as a planned tandem or as salvage for relapse.

**Conclusions**—Our results suggest that second allogeneic HCT is costly, particularly if it follows a prior allogeneic transplant, and is driven by the costs of complications.

### Keywords

Hematopoietic cell transplantation; economics; costs; cost-effectiveness; Pharmacoeconomics

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## INTRODUCTION

In the past, allogeneic transplants subsequent to a previous allogeneic (allo-alo) or autologous (auto-alo) transplant were used exclusively as a therapeutic treatment for graft failure, relapse of disease or occasionally the development of a different malignancy after the initial hematopoietic cell transplantation (HCT).(1) The last decade has also seen a substantial increase in the number of planned tandem auto-alo transplants for the treatment of myeloma and lymphoma, even though the efficacy of this strategy is still a matter of great controversy, especially in myeloma.(2) According to government statistics, HCT generated the greatest percentage increase in total hospital costs from 2004 to 2007, due primarily to an increase in the cumulative number of hospital stays.(3) The increase in number of hospital stays is likely because the procedure is more widely available due to reduced intensity conditioning regimens and better supportive care. This has led to inclusion of older and sicker individuals and the ability to perform multiple transplants in patients. The implementation of the Affordable Care Act may further accelerate the trend since it prohibits the health plans from setting lifetime dollar limits on the benefits, which may have previously limited second transplants. Approximately 15,000 allo-alo and 8300 auto-alo transplants were reported to the Center for International Blood and Marrow Transplant Registry between 2000 to 2010 (personal communication, Tanya Pedersen, CIBMTR, January 2012).

Multiple studies examining patient outcomes after a second allogeneic transplant reported an overall survival in the range of 20 to 40% at 3 years.(4–14) An exception has been planned tandem auto-alo transplants which have shown more favorable complete response rates and survival, though a recent phase III trial in myeloma showed an efficacy comparable to tandem autologous HCT.(15–18)

The decision to pursue a second allogeneic transplant has clinical as well as financial implications. Messori et al have looked at the cost effectiveness of second allogeneic bone marrow transplantation in patients with relapsed acute leukemia based on published data from January 1985 to June 1998.(19) They showed that second HCT prolonged survival and was cost effective as compared to chemotherapy for relapse after an initial HCT. However the authors did not report a detailed analysis of costs in their report. Our study aimed to evaluate the clinical and economic outcomes of a second allogeneic HCT following a prior autologous or allogeneic transplant. We specifically sought to identify the main factors that are associated with costs in a modern cohort of patients.

## RESULTS

### Clinical characteristics of the study cohort

Table 1 summarizes the demographic, disease and transplant-related characteristics of the 245 patients. Median age at second HCT was 50 years (range, 21–68 years) in the allo-alo group and 51 years (range 18–72 years) in the auto-alo group. Three fifths of the study population was male in both groups. Median follow-up period from HCT was 19.8 months (range, 0.5–61.2 months).

### Clinical Events and Outcomes

Engraftment occurred in 230 out of 245 patients and the median time to an absolute neutrophil count of  $500/\mu\text{l}$  was 15 days (range, 6–49 days). The other clinical outcomes of GVHD, organ toxicity, relapse and causes of death for the first 100 days are shown in Table 2. One year transplant-related mortality in this cohort was 15% and the relapse rate was 36%. Figure 1 show the overall survival curves for the allo-alo and auto-alo groups according to the reason for second transplant.

## Costs and predictors of costs

Table 3A shows the median costs for the first 100 days (30 days for the autologous HCT) after the first and second HCT. In the subset of the allo-alo group for which we had data for both transplants, the second allogeneic HCT was more expensive than the first (median 156,000 vs. 132,000;  $p = 0.03$ ). Various categories of the costs are reported in table 3B.

In the multivariate analyses for the allo-alo group, there was no association of costs with age, disease, disease status, or conditioning regimen though graft failure as a reason for HCT was associated with higher costs when only pre-transplantation variables were considered. Use of myeloablative conditioning and unrelated or mismatched donors was a significant cost driver in the auto-alo group, but not in allo-alo group, in the model using only pre-transplant variables. Only mismatched donors remained significant when both pre and post-transplantation variables were considered. Among the post-transplant complications, acute GVHD, pulmonary complications and infection were associated with significantly increased costs in both groups while renal complications were significant only for the allo-alo group. Interestingly, while the year of transplant was associated with a 14% *decrease* in costs per year in the allo-alo group, a 4% *increase* per year was seen in the auto-alo group. (Table 4A and B)

We also analyzed the costs in the auto-alo group ( $n = 110$ ) after excluding the planned tandem auto-alo transplants and found that the magnitude and direction of the effects was similar but some previously significant findings were no longer significant, likely due to the loss of power associated with the smaller sample size. The sole substantive difference was that transplant costs for myeloma were higher when planned tandem transplants were excluded, though not statistically significant in either case. The costs and predictors of costs for the auto-alo group after excluding the planned tandem transplants are shown in the supplemental digital content table 1 and 2.

## DISCUSSION

Second allogeneic HCT has been used as a therapeutic strategy to address relapse, graft failure or second malignancy after a prior HCT, or to try to achieve better disease control as part of planned tandem transplant after a prior autologous procedure. Our study evaluated two distinct cohorts of second allogeneic HCT (allo-alo and auto-alo) for costs of second HCT and described their association with pre-transplant characteristics and post-transplant complications. Similar to what has been shown for first HCT; we found that baseline patient characteristics do not help predict the costs except for mismatched donor transplants which were associated with higher costs in the auto-alo group. Additionally, post-transplant complications are significant cost drivers for second HCT in both the groups.(20) The outcomes of a second allogeneic HCT after a prior allogeneic HCT have generally been quite disappointing.(4) High transplant related mortality (TRM), ranging from 30 to 60%, is reportedly due to post-transplant infections and regimen related toxicity which is higher than with first transplants.(7, 8, 11, 12, 21) Our study shows that these complications also increase the cost of the procedure significantly. In the allo-alo group, the second HCT was more expensive than the first allogeneic procedure ( $p = 0.03$ ), even though the overall costs for the second HCT are still in the range of reported costs in prior studies.(22) There was no evidence that this cost difference was dependent on the interval between the two transplants being less than or greater than 100 days ( $p = 0.88$ ).

Our study also described the outcomes and costs of allogeneic HCT following an autologous HCT. Similar to the allo-alo group, the overall costs for the autologous and allogeneic HCT are in the range of what has been described in the literature.(22) Interestingly, while there was a difference in costs between second HCT when done as a planned tandem auto-alo or

for relapse of disease after a prior autologous HCT in univariate analysis (data not shown), this distinction lost its significance in the multivariate analysis, likely due to adjustment for patient and disease related characteristics. The cost multipliers were similar in magnitude and direction for most variables (except for pulmonary complications and multiple myeloma) when the planned tandem auto-allo transplants were excluded.

A cost-effectiveness analysis using the upper range of published cost data from 1992 to 1996 for HCT showed an acceptable cost profile for second HCT done for relapse of leukemia as compared to chemotherapy.(19) The sensitivity analysis in this study explored the consequences of varying HCT costs and found that the cost per life year gained remained close to the acceptable threshold of \$50,000 per quality adjusted life year gained if the transplant costs were \$150,000 (\$184,688 in 2010 dollars). A more recent descriptive cost study by Svahn et al showed that re-transplantation is associated with higher mean costs of the first HCT itself (relative hazard 1.21,  $p = 0.001$ ), though the costs for second transplant were not separated from the first transplant.(23) This is similar to the solid organ literature where re-transplantation has also been shown to be associated with greater costs and worse survival, raising important ethical questions due to depletion of already limited supply of organs.(24) While the ethical dilemma is not quite as poignant in the field of blood and marrow transplantation since the graft is usually not a limited resource, the question about high costs, optimum use of societal resources and ethics of second HCT has been raised by investigators.(6, 25)

In this era of increasing health care costs, consideration of second HCT especially for relapse should be made based on clinical effectiveness and economic impact of the projected outcome to optimize the utility of our scarce resources. This is especially relevant if non-transplant options may be available with no convincing evidence for one approach being better than others. Similarly, for the tandem auto-allo transplants, doing them outside a clinical study may result in widespread use before evidence of their effectiveness is available. This risks a similar experience as with the use of high dose therapy and autologous transplants for breast cancer, where public opinion, political influence and the threat of litigation resulted in coverage of this procedure by insurance companies even though eventually definitive clinical trial data showed no overall benefit and greater toxicity. (26)

Our study does have some limitations. The study is from a single center and the sample size was limited in the allo-allo group though still bigger than most single center studies reporting on clinical outcomes of second HCT. This may have prevented our ability to detect any associations between costs and clinical characteristics. We were missing some details that would have been helpful, such as information about co-morbidities and uniform follow-up cost data beyond day 100, since most patients return to the care of their local physician beyond 100 days. It is unknown if the rate of complications beyond 100 days is higher for second HCT since that would imply higher downstream costs also. We did not conduct a cost-effectiveness analysis because we could not analyze costs of patients who were managed without a second transplant. Also, there are no randomized trial data available to estimate survival with and without a second transplant. Modeling survival estimates from published literature would be dubious because of the limited follow-up and only small amount of information being available. Because this was a retrospective study, we did not have any information about financial burden of the second HCT on patients and their families. Finally, the cost estimates reflect resource utilizations at our center and may not be representative because of differences in practice patterns, patient mix and accounting methodologies at different centers.

Despite the above limitations, our study provides valuable information that can be used to design economic analyses comparing prevention or treatment of relapse, graft failure or second malignancy vs. second HCT. This study is one of the first to provide economic data on the tandem auto-allo transplants to build a framework for the economic assessment of this strategy. It provides estimates of direct medical costs to help design a cost-effectiveness analysis comparing the planned approach to salvage HCT for relapse. Finally, it characterizes the factors that are associated with higher costs of second HCT to help design interventions that would help improve clinical outcomes while helping to contain the costs. Efforts to improve the clinical outcomes further by decreasing the regimen related toxicity and recurrence rates of second transplant can not only help lower costs, but also improve the cost-effectiveness of the procedure further.

Our results suggest that the short-term costs of second transplants appear higher than those of first transplants especially for allo-allo transplants and the clinical outcomes have much room for improvement. Additional work is needed with larger numbers of patients to confirm the characteristics that would predict the group with the best clinical and economic outcomes. A careful assessment of both benefits and costs of expensive medical interventions such as second HCT is paramount for providing high-value and high-quality care and allow optimum allocation of the finite resources.

## PATIENTS AND METHODS

### Patients

This retrospective study included 245 patients who underwent an allogeneic transplant following a prior autologous or allogeneic HCT between 2004 and 2010 at a single large center. Patients gave consent allowing the use of medical records for research, and the Institutional Review Board at the Fred Hutchinson Cancer Research Center (FHCRC) approved the study.

Eighty four patients received their first transplant at another center, so the details and costs of the prior procedure were not available. In the allo-allo group, the second HCT was performed for recurrence of the original disease in 65% of patients and for graft failure in 25%. Fifty four percent of patients in the auto-allo group received the second HCT for relapsed disease, and 42% were planned tandem auto-allo transplants. For the remaining patients in both groups, the second HCT was done for a different indication than the original diagnosis (e.g., aplastic anemia after initial transplant for acute myeloid leukemia, treatment related myelodysplastic syndrome/ acute myeloid leukemia following an autologous HCT). The median time between the first and second transplantations was 12.8 months (range, 1.5–186.2) in the allo-allo group and 9.6 months (range, 1.3–167.8 months) in the auto-allo group.

### Conditioning, GVHD prophylaxis and supportive care for the second HCT

Myeloablative conditioning was used more frequently for the second HCT in the allo-allo group as compared to the auto-allo group (40% vs. 27%,  $p = 0.07$ ) Patients with aplastic anemia (AA) received cyclophosphamide and antithymocyte globulin. Graft vs. host disease (GVHD) prophylaxis was per protocol and antimicrobial prophylaxis, blood product and nutritional support were provided per institutional guidelines.

Most non-myeloablative/ reduced intensity transplants were performed as outpatients with hospital admission only for cell infusion (if mandated by insurance or for stem cell products arriving when the outpatient clinic was closed). Patient were admitted to the hospital primarily for management of complications such as febrile neutropenia, severe GVHD

requiring parenteral nutrition and iv medications, severe pain requiring intravenous narcotics, inability to maintain oral intake etc.

Patients receiving myeloablative regimens were admitted prior to the cell infusion or during the conditioning depending on the regimen, and discharge criteria were based on neutrophil engraftment, adequate oral intake, and medical stability.

### Cost data

All charges (inpatient and outpatient) and total hospital days for the second HCT from D -7 of transplant to D+100 were retrieved from the administrative database. This information was also retrieved for the first HCT for patients who had received their first HCT at our institution. For the first autologous HCT, D -7 to D+30 was used as the time horizon for costs. If the interval between the two transplants was shorter, the upper limit for the first HCT costs was considered d -8 of the second HCT. Charges were converted to costs using departmental ratios of charges to costs and adjusted to the year 2010 using the medical care component of the consumer price index.(27) This methodology was used since our administrative database employs the traditional system of cost allocation and has only started to implement activity based costing which provides a more accurate estimates of costs. Costs of donor identification and graft procurement were excluded. Professional charges, patient time and productivity costs, costs of prescription medications and direct non-medical costs (e.g. transportation, lodging) were not captured.

### Statistical Analysis

Cumulative incidence estimates were calculated for relapse, acute GVHD, and non-hematological toxicity, treating death as a competing risk. Cumulative incidence estimates of non-relapse mortality treated relapse as a competing risk. Overall survival was estimated using the Kaplan-Meier method. A descriptive analysis of the inpatient and outpatient costs for the first 100 days was done using numeric summaries (mean, variance, median, range). Pre-transplant and post-transplant predictors of costs were identified using multiple linear regression with year of transplant, patient (e.g. demographics, disease variables, CMV status) and transplant characteristics (e.g. stem cell source, HLA matching, donor type, conditioning regimen) entered first, and post-transplant complications (severe infections, VOD, pulmonary or renal complications) added second. Separate models were created for the allo-allo and the auto-allo groups.

Since distribution of costs is typically right skewed, the logarithm of costs was used for the multivariate analysis. Results are presented as 'cost multipliers' which are the ratios of costs of patients with specific baseline characteristics or experiencing the specific complication compared with those who do not. For example, a cost multiplier of 1.17 for relapse corresponds to a 17% increase in costs of patients who relapsed as compared to those who did not. Separate analyses were done for the auto-allo group after excluding the planned tandem transplants. All reported p-values are two-sided and p-values less than 0.05 were considered significant.

### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

<b>AA</b>	aplastic anemia
<b>ALL</b>	acute lymphoid leukemia
<b>AML</b>	acute myeloid leukemia
<b>BM</b>	bone marrow
<b>CLL</b>	chronic lymphocytic leukemia
<b>CMV</b>	Cytomegalovirus
<b>D</b>	donor
<b>GVHD</b>	graft vs. host disease
<b>HCT</b>	Hematopoietic cell transplantation
<b>HD</b>	Hodgkin's disease
<b>MA</b>	myeloablative
<b>MDS</b>	myelodysplastic syndrome
<b>MPD</b>	myeloproliferative disease
<b>NHL</b>	non-Hodgkin's lymphoma
<b>NMA</b>	non-myeloablative
<b>PBSC</b>	peripheral blood stem cell
<b>R</b>	recipient
<b>SOS</b>	sinusoidal obstruction syndrome

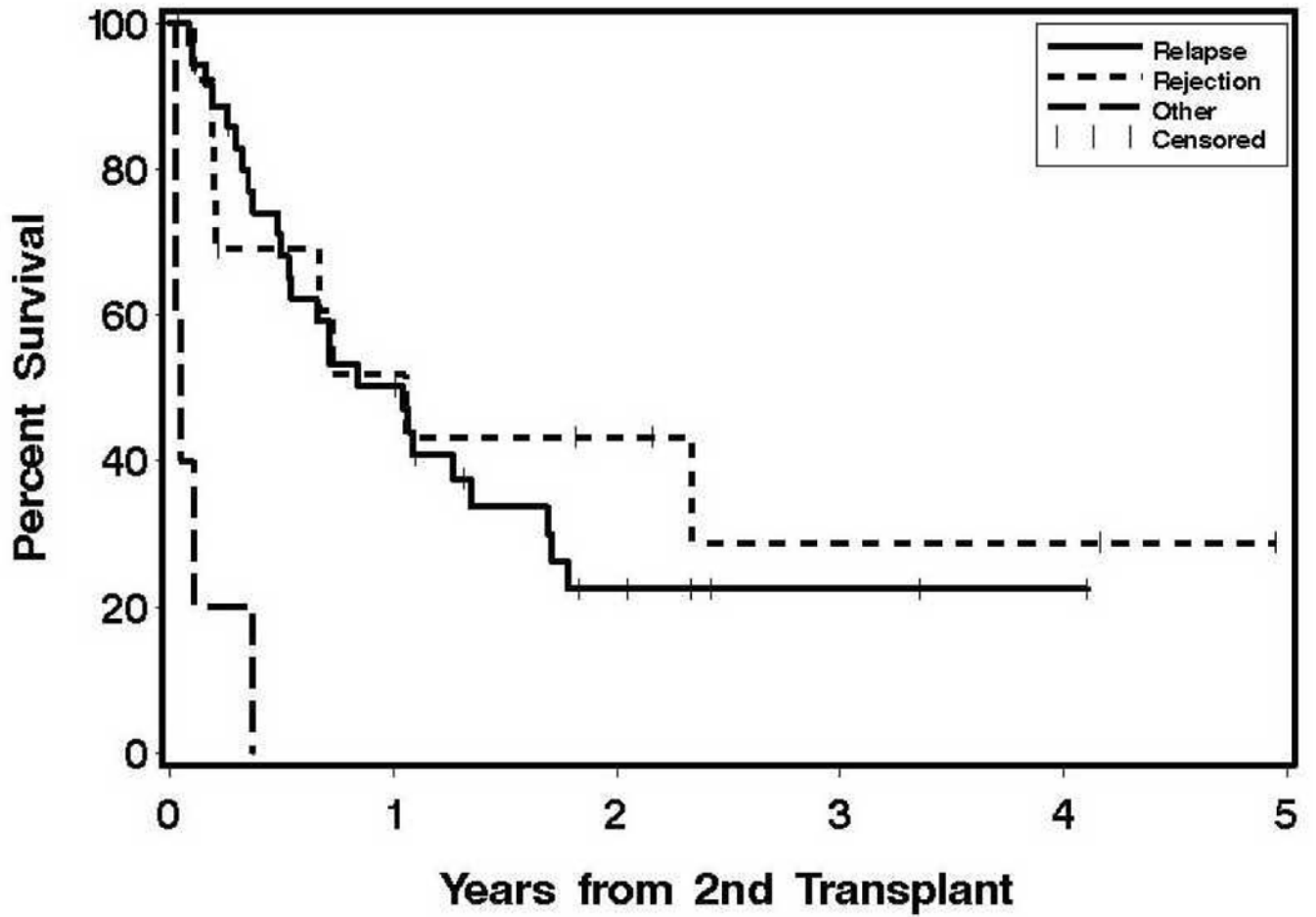
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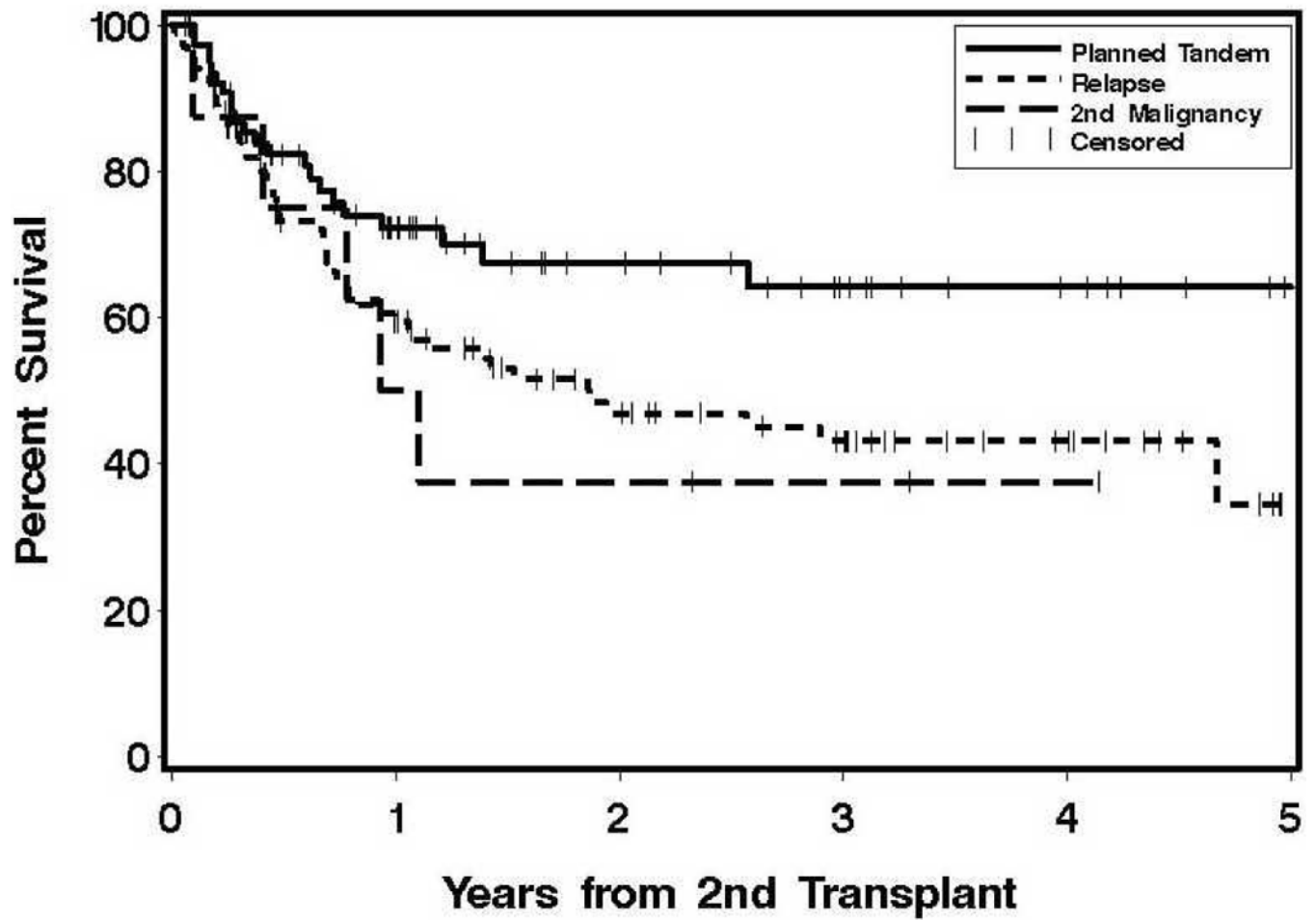
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**Figure 1. Overall survival according to the indication for second hematopoietic cell transplant**

A) Second allogeneic HCT following a prior allogeneic transplant

B) Second allogeneic HCT following a prior autologous transplant

**Table 1**

## Baseline clinical characteristics

Characteristic	Allo-Allo (n = 55)	Auto-Allo (n = 190)
Age (years)		
Median (range)	50 (21–68)	51 (18–72)
Males	34 (62)	114 (60)
Diagnosis		
AML/MDS/MPD	38 (69)	21 (11)
ALL	7 (13)	2 (1)
NHL/HD/CLL	6 (11)	108 (57)
Multiple Myeloma	0	59 (31)
Other	4 (7)	0
Reason for second transplant		
Tandem	0	80 (42)
Relapse	36 (65)	102 (54)
Graft failure	14 (25)	0
Other reasons including second malignancy	5 (9)	8 (4)
Disease status (3 missing)		
Relapse	22 (40)	134 (71)
Remission	33 (60)	56 (29)
Donor		
Matched related	10 (18)	72 (38)
Matched unrelated	31 (56)	63 (33)
Mismatched	14 (25)	55 (29)
Conditioning		
High intensity	22 (40)	52 (27)
Reduced intensity/Non-myeloablative	33 (60)	138 (73)
Stem cell source		
PBSC	44 (80)	160 (84)
BM	5 (9)	28 (15)
Cord	6 (11)	2 (1)
CMV serostatus (7 missing)		
D+/R–	5 (10)	22 (12)
D+/R+	16 (32)	50 (27)
D–/R–	13 (26)	57 (30)
D–/R+	16 (32)	58 (31)
Months between transplants		

Characteristic	Allo-Allo (n = 55)	Auto-Allo (n = 190)
Median (range)	12.8 (1.5–186.2)	9.6 (1.3–167.8)

Abbreviations: HCT, Hematopoietic cell transplantation; Allo-allo, 2 allogeneic transplants; Auto-allo, autologous transplant followed by allogeneic transplant; AML, acute myeloid leukemia; MDS, myelodysplastic syndrome; MPD, myeloproliferative disease; ALL, acute lymphoid leukemia; NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease; CLL, chronic lymphocytic leukemia; PBSC, peripheral blood stem cell; BM, bone marrow; CMV, Cytomegalovirus; D, donor; R, recipient

**Table 2**

Clinical outcomes in first 100 days after second HCT

Variable N (%)	Allo-allo (n = 55)	Auto-allo (n = 190)
Cumulative incidence of relapse	14 (25)	40 (21)
Cumulative incidence of grades II-IV acute GVHD	34 (62)	128 (67)
Regimen related toxicity ( grade 3)/ Infections		
Pulmonary	10 (18)	29 (15)
Veno-occlusive disease/sinusoidal obstructive syndrome	8 (15)	10 (5)
Renal/bladder	9 (16)	79 (42)
Infections	29 (53)	117 (62)
Number of deaths	13 (24)	24 (13)
Cause of death <sup>1</sup>		
Relapse	3 (23)	3 (33)
Graft-vs.-Host disease	1 (7)	5 (20)
Infection	5 (38)	6 (25)
Other	5 (38)	9 (38)

Abbreviations: HCT, Hematopoietic cell transplantation; Allo-allo, 2 allogeneic transplants; Auto-allo, autologous transplant followed by allogeneic transplant

<sup>1</sup>Sum of percentages > 100% since multiple causes of death were listed for some patients



**Table 3A**

Costs, length of stay and cost-categories

Costs and length of stay for the first 100 days after the first and second HCT

	Allo-allo		Auto- allo	
	1 <sup>st</sup> Allo (n = 42)	2 <sup>nd</sup> Allo (n = 55)	Auto <sup>I</sup> (n = 119)	Allo (n = 190)
Median total costs, \$1000's (range)	132 (25–279)	151 (62–405)	72 (28–167)	109 (26–490)
Median Inpatient costs, \$1000's (range)	76 (0–278)	92 (0–371)	43 (0–128)	22 (0–433)
Median Outpatient costs, \$1000's (range)	60 (1–155)	68 (0–194)	29 (3–88)	72 (1–199)
Median hospital stay, days (range)	25 (0–47)	23 (0–76)	15 (0–34)	9 (0–96)

<sup>I</sup>For first 30 days after the autologous HCT

Abbreviations: Allo-allo, 2 allogeneic transplants; Auto-allo, autologous transplant followed by allogeneic transplant

**Table 3B**

Categories of costs (percent of total costs) in the allo-allo and auto-allo group

	<b>Allo-allo</b>	<b>Auto-allo</b>
Outpatient	12%	19%
Inpatient	29%	21%
Pharmacy	20%	19%
Laboratory/ pathology	15%	21%
Radiology/ diagnostics	3%	6%
Transfusion	11%	7%
Miscellaneous	10%	7%

Abbreviations: Allo-allo, 2 allogeneic transplants; Auto-allo, autologous transplant followed by allogeneic transplant

**Table 4A**

Linear regression for costs  
Allogeneic HCT following a prior allogeneic transplant

Variable	Baseline model			Full model		
	Cost multiplier	95% CI	P value	Cost multiplier	95% CI	P value
Pre-transplant factors						
Age						
< 50	1.0			1.0		
50	1.01	0.77–1.32	0.96	1.03	0.80–1.33	0.81
Disease						
Acute leukemia/MDS	1.0			1.0		
Lymphoma	1.07	0.68–1.68	0.77	0.89	0.59–1.34	0.57
Other	0.61	0.33–1.11	0.11	0.67	0.39–1.15	0.15
Disease status						
Remission	1.0			1.0		
Relapse	0.89	0.64–1.25	0.51	0.84	0.61–1.15	0.29
Graft source						
PBSC	1.0			1.0		
BM/Cord	1.27	0.83–1.94	0.28	1.36	0.92–1.99	0.13
Conditioning						
NMA	1.0			1.0		
MA	1.39	0.96–2.03	0.09	1.23	0.88–1.72	0.24
Reason for transplant						
Relapse	1.0			1.0		
Rejection/failure	<b>1.41</b>	<b>1.01–1.97</b>	<b>0.05</b>	1.25	0.93–1.69	0.14
Other	1.00	0.57–1.76	0.99	0.96	0.54–1.72	0.90
Year of transplant						
Per year	0.96	0.86–1.07	0.45	<b>0.86</b>	<b>0.78–0.95</b>	<b>0.005</b>

Variable	Baseline model			Full model		
	Cost multiplier	95% CI	P value	Cost multiplier	95% CI	P value
Donor type						
Matched related	1.0			1.0		
Matched unrelated	0.97	0.68–1.37	0.86	0.91	0.67–1.22	0.52
Mismatched (related and unrelated)	1.00	0.63–1.59	0.99	0.77	0.51–1.18	0.24
Patient CMV serostatus						
Negative	1.0			1.0		
Positive	1.01	0.76–1.35	0.94	0.87	0.67–1.13	0.30
Post-transplant complications						
Death				0.70	0.46–1.06	0.10
Relapse				1.20	0.90–1.60	0.23
GVHD (II-IV)				<b>1.42</b>	<b>1.09–1.84</b>	<b>0.01</b>
SOS				0.92	0.63–1.33	0.66
Pulmonary				<b>1.55</b>	<b>1.12–2.16</b>	<b>0.01</b>
Renal				<b>1.90</b>	<b>1.16–3.10</b>	<b>0.02</b>
Infection				<b>1.42</b>	<b>1.10–1.85</b>	<b>0.01</b>

Abbreviations: MDS, myelodysplastic syndrome; PBSC, peripheral blood stem cells; BM, bone marrow; NMA, non-myeloablative; MA, myeloablative; CMV, cytomegalovirus; GVHD, graft vs. host disease; SOS, sinusoidal obstruction syndrome

**Table 4B**

Allogeneic HCT following a prior autologous transplant

Variable	Baseline model			Full model		
	Cost multiplier	95% CI	P value	Cost multiplier	95% CI	P value
Pre-transplant factors						
Age						
< 50	1.0			1.0		
50	1.04	0.91–1.18	0.58	1.02	0.91–1.15	0.68
Disease						
Lymphoma	1.0			1.0		
Acute leukemia/MDS	1.05	0.81–1.35	0.71	1.09	0.87–1.36	0.47
Myeloma	0.87	0.74–1.02	0.09	0.94	0.82–1.09	0.44
Disease status						
Remission	1.0			1.0		
Relapse	1.07	0.91–1.25	0.40	1.03	0.90–1.19	0.66
Graft source						
PBSC	1.0			1.0		
BM/Cord	0.97	0.73–1.28	0.81	0.92	0.72–1.18	0.52
Conditioning						
NMA	1.0			1.0		
MA	<b>1.23</b>	<b>1.00–1.51</b>	<b>0.05</b>	1.13	0.94–1.35	0.21
Reason for transplant						
Relapse	1.0			1.0		
Tandem auto-allo	0.93	0.80–1.09	0.37	0.93	0.81–1.06	0.26
Secondary malignancy	0.78	0.53–1.14	0.20	0.82	0.59–1.15	0.25
Year of transplant						
Per year	<b>1.05</b>	<b>1.01–1.10</b>	<b>0.02</b>	<b>1.04</b>	<b>1.01–1.08</b>	<b>0.03</b>

Variable	Baseline model			Full model		
	Cost multiplier	95% CI	P value	Cost multiplier	95% CI	P value
Donor type						
Matched related	1.0			1.0		
Matched unrelated	<b>1.23</b>	<b>1.05–1.45</b>	<b>0.01</b>	1.12	0.97–1.29	0.12
Mismatched (related and unrelated)	<b>1.34</b>	<b>1.10–1.62</b>	<b>0.004</b>	<b>1.19</b>	<b>1.00–1.42</b>	<b>0.05</b>
Patient CMV serostatus						
Negative	1.0			1.0		
Positive	1.10	0.96–1.25	0.17	1.01	0.89–1.13	0.91
Post-transplant complications						
Death				1.06	0.87–1.29	0.55
Relapse				1.02	0.89–1.18	0.73
GVHD (II-IV)				<b>1.15</b>	<b>1.02–1.30</b>	<b>0.03</b>
SOS				0.93	0.71–1.22	0.61
Pulmonary				<b>1.42</b>	<b>1.19–1.71</b>	<b>0.0002</b>
Renal				1.01	0.90–1.14	0.82
Infection				<b>1.38</b>	<b>1.21–1.57</b>	<b>&lt; 0.0001</b>

Abbreviations: MDS, myelodysplastic syndrome; PBSC, peripheral blood stem cells; BM, bone marrow; NMA, non-myeloablative; auto-allo, autologous transplant followed by allogeneic transplant; CMV, cytomegalovirus; GVHD, graft vs. host disease; SOS, sinusoidal obstruction syndrome