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Acute myeloid leukaemia relapsing after allogeneic haematopoietic stem cell transplantation:
prognostic factors and impact of initial therapy of relapse

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Contributions

A.B.M.L. and D.R. wrote the manuscript. A.B.M.L., D.R. and G.K. designed the analysis. A.B.M.L., C.C., C.Y.F., I.B., A.B., D.P., B.G., A.M.J., T.A., and K.F. collected and interpreted clinical data. A.B.M.L. and M.C. conducted the statistical analysis. All authors contributed to manuscript editing.

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MAIN BODY TEXT

BACKGROUND

Acute myeloid leukaemia (AML) is the most common indication for allogeneic haematopoietic stem cell transplantation (alloHSCT) in adults in Australia, as well as the United States and Europe.¹⁻³ Registry studies report long-term post-alloHSCT survival in AML of 20-50% depending on donor source and disease risk.¹⁻² Despite the ability for alloHSCT to reduce the relapse risk in patients with AML, the main cause of treatment failure remains relapse. The cumulative incidence of relapse after alloHSCT for AML in first complete

remission (CR) is 25-35% for intermediate cytogenetic risk AML, and 50-60% for poor cytogenetic risk AML.⁴⁻⁷

Whilst patients with AML relapsing after alloHSCT have a poor prognosis, potential for cure remains in a minority of patients, resulting in overall survival (OS) of 10-20% at two years from time of relapse.⁸⁻¹³ Long-term remission appears to rely on therapies that maximise the graft-versus-leukaemia effect (GVL).¹⁴⁻¹⁵ However it is unclear whether chemotherapy (CT) is a prerequisite to donor cell-based therapy (DCT) such as donor lymphocyte infusions (DLI) or re-transplantation. Similarly, determining who might benefit most from salvage for AML relapse post-alloHSCT is difficult as some patients with potentially curable AML may receive ineffective therapy, whilst others unlikely to derive benefit from intervention are exposed to expensive and ultimately futile interventions.

With the incorporation of effective molecular risk stratification in AML, and increasing use of both T-cell depletion and reduced intensity conditioning, the current ability for patients to be salvaged from relapse after alloHSCT may have altered from that described historically. Furthermore, recent data suggests that the association between GVHD and GVL may be weakest in AML compared to other diseases, and that mechanisms of GVL in AML may be independent of those of GVHD, raising the possibility that absence of GVHD prior to relapse may not be predictive of salvage outcome.¹⁶

To better understand the patient and disease variables that might determine successful salvage therapy for population we undertook a retrospective analysis of Australian patients who had AML relapse after prior alloHSCT. We focused on the impact of GVHD pre- and post-alloHSCT as a predictor for improved survival.

MATERIALS AND METHODS

Patients

Nine Australian alloHSCT centres contributed data on patients who had relapsed after an alloHSCT for AML, with a transplant date between 1 January 2000 and 31 December 2011 inclusive. Patients with acute promyelocytic leukaemia or prior chronic myeloid leukaemia were excluded.

Centres provided data on age, sex, pre-transplant variables (*de novo* or secondary/transformed AML, cytogenetics, FLT3-ITD mutation status, prior induction failure), transplant variables (transplant date, disease status at transplant, donor relation, donor gender, graft source, HLA matching, conditioning type and intensity, use of T-cell depletion), variables at relapse (date of first relapse, presence of extramedullary disease, marrow blast percentage at relapse, prior acute GVHD [aGVHD] or chronic GVHD [cGVHD] and grade), and details of subsequent treatment (if any was given, whether any of CT, radiotherapy, DCT and interferon- α were used, responses to CT, use of conditioning and/or immunosuppression with DCT) and outcome including further progression and dates of death or last follow-up.

Definitions

Induction failure was defined as to failure to attain CR after one cycle of high-dose cytarabine or after two courses of standard-dose cytarabine. Cytogenetic risk and conditioning intensity were classified according to published guidelines.¹⁷⁻¹⁸ CR was defined as less than 5% marrow blasts.¹⁹ Relapse post-alloHSCT was defined as re-emergence of morphologic AML, based on peripheral blood or marrow morphology, or cytology and/or histology of an extramedullary specimen, after prior CR.

Salvage therapy was defined as any of DCT; interferon; salvage CT including at least standard-dose cytarabine or gemtuzumab ozogamicin; or radiotherapy in the case of relapse limited to extramedullary sites. Intrathecal chemotherapy alone for the treatment of isolated central nervous system relapse of AML was not regarded as salvage therapy. Due to inadequate data, immunosuppression withdrawal alone was not considered salvage therapy.

DCT was defined as either second alloHSCT or DLI. DLI was defined as receipt of donor cells without conditioning, whereas second alloHSCT was defined as receipt of donor cells immediately preceded by chemotherapy.

Acute and chronic GVHD were graded according to accepted criteria.²⁰⁻²² Limited cGVHD according to the Shulman criteria was grouped with mild cGVHD according to the NIH criteria, while extensive cGVHD was grouped with moderate to severe cGVHD according to the Shulman and NIH criteria respectively.

OS from relapse (OSR) was defined as the time from the date of first relapse post-alloHSCT, to the date of death or last follow-up.

Statistical analysis

Median follow-up was calculated using the reverse Kaplan-Meier method.²³ Differences in categorical variables were tested with Fisher's exact test and differences in unpaired variables tested with the Wilcoxon rank-sum test. Differences in median follow-up were calculated using the logrank test.²⁴

The primary endpoint of the study was OSR, analysed using the Kaplan-Meier product-limit method.²⁵ Differences between groups were tested using the logrank test. Post-relapse GVHD, when evaluated for its effect on OSR, was regarded as a time-dependent covariate. Multivariate models were constructed using the Cox proportional hazards model and a manual backwards stepwise selection process.

Post-relapse GVHD, when evaluated as an endpoint, was measured using cumulative incidence estimation, with subsequent relapse and death without further relapse regarded as competing risks. Differences in cumulative incidences were tested using the method of Gray, and multivariate analysis was conducted using competing risks regression.²⁶

Calculations were performed using R (version 3.0.1; cran.r-project.org) on the RStudio platform (version 0.97.551; Free Software Foundation, Boston, Mass.).

RESULTS

Patients

From 1338 first alloHSCTs performed for AML between 2000 and 2011, 386 patients were identified as having relapsed after alloHSCT. 37 patients had insufficient data for survival analysis. The median follow-up for the remaining 349 patients was 39.3 months (range 0.1-118.2 months). The median time to relapse from alloHSCT was 5.5 months (range 0.2-123.1 months). The five-year OSR was 9% (95% CI 7-14%) for all patients. Baseline characteristics of the cohort are described in Table 1, and details of relapse are presented in Table 2.

Factors predicting outcome

Results of univariate analysis for the cohort are presented in Table 3. The multivariate Cox model of best fit yielded two variables that remained independently associated with inferior OSR: time to first relapse less than six months (HR 2.4, 95% CI 1.9-3.1, $P < .001$), and the presence of grade 3-4 aGVHD prior to first relapse (HR 2.0, 95% CI 1.4-2.8, $P < .001$). Primary induction failure, bone marrow blast percentage $> 30\%$, extramedullary relapse, and chronic GVHD prior to relapse were significantly associated with OSR on univariate analysis but were no longer significant on multivariate analysis.

Proposed prognostic index

For the prognostic index for risk stratification from the time of first relapse, each patient in the cohort was assigned a score giving one point for time from first alloHSCT to first relapse post-alloHSCT less than six months, and one point for any grade 3-4 aGVHD prior to first relapse.

Of the 349 patients in the cohort, 138 patients scored zero, 157 patients scored one, and 23 patients scored two. 31 patients had insufficient data for scoring and were excluded from analysis. Five-year OSR was 18% (95% CI 12-27%), 4% (2-10%), and 0%, for patients who scored zero, one and two respectively. The HR for mortality for patients who scored greater than zero was 2.3 (95% CI 1.8-2.9, $P < .001$; Figure 1).

When the cohort was restricted to the 197 patients who received any form of salvage therapy, five-year OSR was 22% (95% CI 15-33%) for the 111 patients who scored zero compared to 5% (95% CI 4-23%) for the 81 patients who scored greater than zero (HR 1.8, 95% CI 1.3-2.5, $P < .001$). Five patients were excluded due to inadequate data.

Outcome following first relapse post-alloHSCT according to therapy

The outcomes of the 386 patients in the whole cohort, according to therapy given, are shown in Figure 2. Of the 333 patients with known information on whether salvage therapy was given, 199 patients (60%) received salvage therapy. Of the 134 patients that did not receive salvage therapy, 127 patients (95%) had died at a median of 1.1 months (range 0.1-86.2 months). Patients who did not receive any salvage therapy had significantly inferior OSR, with five-year OSR 2% (95% CI 0-7%) vs 14% (95% CI 10-21%) (HR 3.8, 95% CI 3.0-4.9, $P < .001$) (Figure 3). Of the seven survivors among those not receiving salvage therapy, two survived long-term (37 and 103 months) post-relapse following withdrawal of immunosuppression alone and subsequent development of severe chronic GVHD.

Outcomes following reinduction chemotherapy

Of 92 patients with adequate outcome data who received CT at first relapse, 36 (39%) achieved CR or CRi. 18 (20%) had a partial response (PR) – a reduction of blast percentage by 50%, and/or partial resolution of extramedullary disease, without CR – and 36 (39%) had no response. Two patients died during reinduction. The median time from relapse to delivery of CT was 11 days (range, 1-206 days). No difference was observed in time to delivery of CT between those achieving CR, PR and no response. To account for response assessment a landmark analysis at 35 days after commencement of CT was performed. OS from landmark for patients achieving CR/CRi was superior to those who did not achieve CR (HR 0.4, 95% CI 0.2-0.7, $P < .001$).

No difference was seen between patients who received DCT consolidation after CR to CT, versus those who achieved CR to CT but did not receive DCT thereafter (HR 0.6, 95% CI 0.3-1.3, $P = .196$). No difference in OS from landmark was observed between the 11 second alloHSCT patients and the six DLI patients (HR 0.8, 95% CI 0.2-2.7, $P = .748$).

Outcomes following donor cell-based salvage used as initial therapy

Of 73 patients with outcome data following DCT, median time from first relapse post-alloHSCT to DCT was 21 days (range 7-184 days). 55 patients received a second alloHSCT and 16 patients received DLI. There was no difference in OSR (HR for second alloHSCT 1.1, 95% CI 0.6-2.2, $P = .697$). Details of conditioning were unknown for two patients.

Comparison of reinduction chemotherapy and donor cell-based therapy as initial therapy

Compared to the DCT cohort, the CT cohort had significantly shorter median follow-up of survivors ($P = .017$), more patients with extramedullary relapse ($P = .020$), and shorter time from relapse to start of salvage therapy ($P < .001$); characteristics were otherwise similar. The median time from relapse to salvage was 10.5 days (range 1-206, interquartile range 5-21.75) for the CT cohort, and 21 days (range 7-184, interquartile range 13-41.25) for the DCT cohort.

To compare CT with DCT as initial therapy of relapse we used a landmark analysis, taking the start time to be the day of commencing salvage therapy. Recipients of CT had significantly inferior OS from salvage (OSS) (HR 1.9, 95% CI 1.3-2.8, $P < .001$), with five-year OSS of 5% (95% CI 2-15%) compared with recipients of DCT, who had five-year OSS of 23% (95% CI 15-37%) (Figure 4). This effect remained significant (HR 2.4, 95% CI 1.6-3.5, $P < .001$) after adjustment for the adverse prognostic features of relapse within 6 months of alloHSCT and history of grade 3-4 aGVHD prior to relapse.

When this analysis was restricted to the patients *without* adverse prognostic features at relapse (ie. patients with relapse beyond 6 months from alloHSCT, with no prior grade 3-4 aGVHD), recipients of CT as initial therapy of relapse had five-year OSS of 9% (95% CI 3-25%) compared with recipients of DCT as initial therapy, who had five-year OSS of 32% (95% CI 20-52%), an approximate doubling of mortality hazard (HR 2.0, 95% CI 1.2-3.3, $P = .007$).

Development of GVHD following salvage therapy

Of 199 patients receiving salvage, 89 did not develop any GVHD post-salvage, 86 developed GVHD post-salvage, and details were unknown for 24 patients. Of the 86 who developed GVHD, 47 developed severe GVHD (defined as grade 3-4 aGVHD or moderate/severe or extensive cGVHD), seven developed non-severe GVHD, and 32 patients had insufficient

information. The presence of post-relapse GVHD of any severity was not associated with a significant improvement in OS compared to patients without post-relapse GVHD (HR 0.8, 95% CI 0.6-1.3, $P = .405$, Figure 5).

DISCUSSION

This study of 386 Australian patients is the largest non-registry analysis of AML relapsing after alloHSCT. Salvage therapy was given to 60% of patients, and of these the majority (93%) received reinduction CT and/or donor cell therapy (be it second alloHSCT or DLI). We observed a five-year survival probability of 14% in salvaged patients, in line with other large studies, highlighting the need for novel approaches in this population. For patients receiving palliation, median survival was five weeks.

We found remission duration post-alloHSCT and prior grade 3-4 acute GVHD to be independent prognostic variables for inferior survival after relapse. These findings are similar to those of the European Group for Blood and Marrow Transplantation's analysis of 263 RIC-alloHSCT recipients with relapsed AML.¹² This comparably powered study found prior acute GVHD of any grade and relapse within five months of alloHSCT, to be prognostic. Other prognostic factors previously identified include performance status at relapse and disease status at time of alloHSCT.^{12,27} Some of these studies include patients with high risk MDS.

Efforts to augment the GVL effect are a cornerstone of salvage therapy in relapsed AML post-alloHSCT. This may be achieved by either DCT or stimulation of engrafted immune effectors by interferon. Predictably we found that these therapies had greater capacity to

induce alloreactivity and GVHD than salvage with CT alone. Notably the cumulative incidence of any GVHD after CT or radiotherapy remained substantial at approximately 20% by one year.

Selection of therapy for AML relapsing after alloHSCT may depend on a number of factors including patient fitness, mode of presentation of relapse (site, leukaemic burden, kinetics), availability of donor lymphocytes, either from the same donor or from a different donor, the presence +/- severity of any GVHD at time of relapse, the degree of immunosuppression at time of relapse, the response to immunosuppression withdrawal and institutional and patient preferences. With the exception of response to withdrawal of immunosuppression, all of these factors are determinable at the time of relapse. Thus we surmised that survival following CT salvage versus DCT salvage could reasonably be compared using an appropriate landmark of time of commencement of salvage.

We found that patients whose first therapy after relapse was DCT had superior OS from start of salvage compared to those receiving CT first. We did not detect imbalances in the groups receiving DCT and CT that might explain the better outcome of patients receiving DCT first, but acknowledge that not all pertinent variables were captured in this study including data relating to immunosuppression and its withdrawal at the time of relapse.

Despite the superior outcome associated with DCT as initial therapy of relapse, we were unable to show a beneficial effect of post-relapse GVHD on survival after AML relapse. Similar findings have been reported by others.¹⁶ This may be due to GVHD-related mortality offsetting any GVL-related survival benefit. Although GVHD of milder severity may have possibly led to a survival benefit as has been observed in registry studies²⁸ the absence of detailed GVHD grading data prevented us from analysing OSR by severity of post-salvage GVHD.

The major limitations of this study were the retrospective nature of the analysis, and missing data. Regarding the former, performance status and therapeutic intent were not captured uniformly, precluding a true assessment of curative versus non-curative management at relapse. Patients with missing data were excluded from certain analyses, hampering statistical power and introducing bias. Also, information on immunosuppression withdrawal was unavailable. This intervention can clearly induce remission and lead to long-term survival as evidenced by two patients who did not receive “salvage” as we defined it.

In summary, we have established a valuable national reference data set for management of patients with AML undergoing alloHSCT. The prognostic indices of relapse within six months and prior grade 3-4 acute GVHD can refine management decisions and inform patients with greater accuracy. More comprehensive data collection of GVHD, therapeutic intent and immunosuppression withdrawal would enhance future analyses in this difficult area, and

the incorporation of our prognostic index in prospective studies of treatment of relapse of AML post-alloHSCT would aid in the analysis of salvage outcomes.

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FIGURES LEGEND

Figure 1. Overall survival after first relapse post-alloHSCT by prognostic index.

Figure 2. Consort diagram of outcomes of all 387 patients with relapse post alloHSCT.

Figure 3. Overall survival after first relapse post-alloHSCT according to whether or not salvage therapy was given post alloHSCT.

Figure 4. Landmark analysis of overall survival according to first type of salvage therapy given for relapse post-alloHSCT.

Figure 5. Overall survival after first relapse post-alloHSCT, according to the presence or absence of GVHD. GVHD is treated here as a time-dependent covariate.

TABLES

Table 1. Characteristics of patients and transplants.

	n	%*
Total number of patients	349	
Female	147	42%
Median age	46	(17-71)
Median follow-up from relapse, all patients, months	39.3	(0.1-118.2)
Disease onset		
De novo	243	70%
Other	87	25%
Prior MDS	48	
Prior CMML	10	
Prior MPN	9	
Secondary	20	
Unknown	19	5%
Cytogenetic risk		
Good	15	4%
Intermediate	218	68%
Poor	98	28%
Unknown	18	5%
Molecular status		
FLT3-ITD mutated	21	33%
FLT3-ITD wildtype	42	67%
Unknown FLT3-ITD mutation status	286	
Disease status		
CR1	164	48%
CR2	54	16%
CR3+	5	1%
PR	35	10%
Refractory, progressive, untreated	87	25%
Unknown	4	
Primary induction failure		

Primary induction failure	96	28%
No primary induction failure	247	72%
Unknown	6	
Graft type		
Mobilised peripheral blood	314	91%
Bone marrow	30	9%
Umbilical cord blood	5	
Donor relation		
Sibling	214	61%
Other relation	9	3%
Unrelated adult	121	35%
Umbilical cord blood	5	1%
Sex matching		
Female donor to male recipient	71	21%
Other sex matching	273	79%
Unknown	5	
HLA matching		
10/10 HLA	302	89%
9/10 HLA	24	7%
8/10 HLA	5	1%
Haploidentical transplant	8	2%
Unknown	10	
Conditioning		
Myeloablative	230	66%
Not myeloablative	117	34%
No conditioning	2	1%
Total body irradiation		
TBI in conditioning	138	40%
No TBI in conditioning	211	60%
T cell depletion		
Any T cell depletion used	71	21%
Thymoglobulin	24	
ATGAM	24	
ATG-Fresenius	16	
Alemtuzumab	5	
Ex vivo T cell depletion	2	
No T cell depletion used	264	79%
Unknown	14	

*Percentages do not include patients with unknown parameters. Some percentages do not add up to 100% due to rounding.

CMML: chronic myelomonocytic leukemia. CR: complete remission. FLT3-ITD: *FMS*-like tyrosine kinase internal tandem duplication. HLA: human leukocyte antigen. MDS: myelodysplastic syndromes. MPN: myeloproliferative neoplasms. PR: partial response.

Table 2. Relapse characteristics.

	n	%*
Total number of patients	349	
Parameters at relapse		
Median days to relapse post alloHSCT	168	(7-3746)
Marrow blast % at relapse	33.8	(0-100)
Not done/dry tap/unknown	142	41%
Extramedullary disease at relapse		
Extramedullary disease at relapse	48	14%
No extramedullary disease at relapse	286	86%
Unknown	15	
Acute GVHD		
Any acute GVHD prior to relapse	181	55%
Maximal grade 1	53	31%
Maximal grade 2	82	48%
Maximal grade 3	23	13%
Maximal grade 4	14	8%
Maximal grade unknown	9	
No acute GVHD prior to relapse	146	45%
Unknown	22	
Chronic GVHD		
Any chronic GVHD prior to relapse	99	31%
Maximal grade limited/mild	47	54%
Maximal grade extensive/moderate/severe	40	46%
Maximal grade unknown	12	
No chronic GVHD prior to relapse	219	69%
Unknown	31	

*Percentages do not include patients with unknown parameters. Some percentages do not add up to 100% due to rounding.

Table 3. Univariate analysis of predictors of overall survival from relapse (OSR).

Risk factor	Control	HR	95% CI	P
Age greater than median (45.5 years)	Age ≤ 45.5 years	1.1	0.9-1.4	.242
Poor cytogenetic risk	Good or intermediate cytogenetic risk	1.2	0.9-1.6	.123
FLT3-ITD mutated	FLT3-ITD wildtype	1.3	0.8-2.2	.236
Secondary/transformed AML	De novo AML	0.9	0.6-1.5	.778
Primary induction failure	No primary induction failure	1.3	1.0-1.7	.029
Not in CR prior to alloHSCt	In CR prior to alloHSCt	1.3	1.0-1.6	.044
Not in CR1 pre alloHSCt	In CR1 prior to alloHSCt	1.2	1.0-1.6	.061
Non-sibling donor	Sibling donor	1.1	0.9-1.4	.351
Reduced intensity or non-myeloablative conditioning	Myeloablative conditioning	0.8	0.7-1.1	.154
TBI in conditioning	No TBI in conditioning	1.2	1.0-1.6	.063
HLA-mismatched donor	HLA-matched donor	1.2	0.9-1.7	.298
Non-peripheral blood graft	Peripheral blood graft	1.1	0.8-1.6	.547
Female donor to male recipient	All other sex match combinations	0.8	0.6-1.1	.176
No T cell depletion	T cell depletion	1.3	1.0-1.7	.083
Bone marrow blasts > 30%	Bone marrow blasts ≤ 30%	1.5	1.1-2.0	.012
Extramedullary relapse	No extramedullary relapse	0.6	0.4-0.9	.006
Time to first relapse < 6 months	Time to first relapse ≥ 6 months	2.3	1.9-3.0	< .001
Time to first relapse < 12 months	Time to first relapse ≥ 12 months	2.2	1.7-2.8	< .001
aGVHD prior to relapse	No aGVHD prior to relapse	1.3	1.0-1.8	.052
Grade 2-4 aGVHD prior to relapse	No grade 2-4 aGVHD prior to relapse	1.4	1.1-1.8	.003
Grade 3-4 aGVHD prior to relapse	No grade 3-4 aGVHD prior to relapse	1.7	1.2-2.5	.002
No cGVHD prior to relapse	cGVHD prior to relapse	1.6	1.3-2.1	< .001
Extensive or moderate-	No extensive or moderate-	0.9	0.6-1.3	.482

severe cGVHD prior to relapse	severe cGVHD prior to relapse			
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aGVHD: acute graft-versus-host disease; alloHSCT: allogeneic haematopoietic stem cell transplant; AML: acute myeloid leukemia; cGVHD: chronic graft-versus-host disease; CI: confidence intervals; CR: complete remission; CR1: first complete remission; HR: hazard ratio; TBI: total body irradiation.

ABSTRACT

Aims

We sought to determine factors associated with overall survival from relapse (OSR) of acute myeloid leukaemia (AML) after allogeneic haematopoietic stem cell transplantation (alloHSCT), and the effect of first salvage therapy and subsequent GVHD on OSR.

Methods

Data on 386 patients from nine Australian centres with relapsed AML post-alloHSCT were collected retrospectively. OSR was calculated using the Kaplan-Meier method. Univariate and multivariate analyses were conducted using the logrank test and proportional hazards modelling respectively, and a prognostic index for OSR was derived from multivariate modelling.

Results

On multivariate analysis, relapse within six months (hazard ratio [HR] 2.4, $P < .001$), and grade 3-4 acute GVHD preceding relapse (HR 2.0, $P = .004$), were associated with inferior OSR. Patients with 1-2 factors had inferior OSR compared to those with zero factors (all patients: HR 2.3, $P < .001$, patients given salvage: HR 1.8, $P < .001$). The first salvage therapy used post-relapse was donor cell therapy (DCT) (second alloHSCT or donor lymphocyte infusion) in 75, reinduction chemotherapy (CT) in 103, radiotherapy in eight and interferon-alfa in six. Although reinduction CT death rate was low (2%), survival after CT was inferior to DCT (HR 1.9, $P < .001$). No survival benefit was seen for patients who developed GVHD following salvage therapy ($P = .405$).

Conclusions

Patients with AML who relapse beyond six months from alloHSCT without prior grade 3-4 acute GVHD have a better outcome from salvage therapy. Salvage treatments employing DCT as initial treatment of AML relapse confer a survival advantage over CT.

IMJ FIGURE1 AMLRelapse OSR by prognostic score.tiff

2nd allo = second allograft (donor cells preceded by conditioning); DLI = donor lymphocyte infusion (donor cells not preceded by conditioning); CR = complete remission; CRi = CR with incomplete count recovery; A+CR = alive and in CR; A+PD = alive with progressive disease (PD); D+CR = death in CR; D+PD = death with PD; RT = radiotherapy.

IMJ FIGURE3 AMLRelapse OSR salvage vs no salvage.tiff

IMJ FIGURE4 AMLRelapse OSS cells vs chemo ALL.tiff

IMJ FIGURE5 AMLRelapse OS by GVHD timedept.tiff

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