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Adoptive immunotherapy via Donor lymphocyte infusions following allogeneic haematopoietic stem cell transplantation for Myelofibrosis: A real world, retrospective multi-centre study.

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Abstract

Allogeneic hematopoietic cell transplantation (allo-HCT) remains the only curative option for Myelofibrosis (MF). Relapse however remains a significant problem in up to 20-30% of cases. Donor Lymphocyte Infusions (DLI) represent a potentially effective strategy for relapse prevention and management, but optimal timing based on measurable residual disease (MRD)/chimerism analyses and regimen choice remain undetermined. We performed a retrospective 'real world' analysis of a multicentre cohort of MF allo-HCT patients from 8 European transplant centres who received DLI between 2005-2022. Response was assessed using IWG-MRT defined response criteria, and survival endpoints were estimated using the Kaplan-Meier estimator and log-rank test. The study included 28 patients with a median age of 58 years and a Karnofsky performance status of >80. The majority of patients had DIPPS-plus Intermediate-2 or high-risk disease at the time of allo-HCT. *In vivo* T cell depletion was utilised in 20 (71.2%) cases, with 19/20 patients receiving anti-thymocyte globulin (ATG). Indication for DLI was either 'pre-emptive' (n=15), due to a decrease in recipient chimerism (n=13) or molecular relapse (n=2), or 'therapeutic' (n=13) for clinician-defined haematological/ clinical relapse. No patient received DLI prophylactically. Median time to DLI administration was 23.4 months post allo-HCT. Of the 16 patients receiving >1 dose of DLI, 12 were part of a planned escalating dose regimen. Median follow-up from time of 1st DLI administration was 55.4 months. Response rates to DLI were CR (n=9), PR (n=1), and clinical improvement (n=6). Chimerism levels improved in 16 patients, and stable disease was reported in 5 patients. No response or progression was reported in 7 patients. DLI-induced aGVHD was reported in 11 (39%) cases, grade 3/4 (n=7;25%). Median overall survival from time of 1st DLI was 62.6 months, and the cumulative incidence of relapse/progression after 1st DLI was 30.8% at 6 months. This study highlights that good response rates can be achieved with DLI even after frank relapse in some patients within a cohort where other treatment options are very limited. More prospective studies are warranted to identify the optimal DLI regimen and timing to improve patient outcomes.

Highlights

- DLI following MF allo-HCT offers a potential option for clinicians if the MRD kinetics are suggestive of imminent relapse or a drop in donor chimerism is detected.

- Clear efficacy of DLI is evident for both mixed chimerism and relapsed MF patients post allo-HCT but should be considered early at the point of molecular relapse if applicable.

- Wider adoption of DLI strategies should be evaluated given the clear efficacy in a challenging setting where no other optimal strategies exist. More prospective studies are warranted to identify the optimal DLI regimen and timing.

Introduction

Allogeneic haematopoietic cell transplantation (allo-HCT) remains the only curative option for Myelofibrosis (MF), achieving an estimated 3-year overall survival of around 50-60% in younger, fit recipients with a matched sibling or unrelated donor (URD)[1,2]. Despite advances, outcomes remain less optimal following use of a HLA-mismatched URD. As regards alternative donor sources, more recent trends highlight increasing utilisation of haploidentical donors,[3] with a move away from the use of umbilical cord blood [4].

The choice of conditioning regimens, intensity and timing of the transplant remain heterogeneous for MF patients and is determined by factors such as transplant centre experience, patient characteristics (age and performance status/ co-morbidities[5]) and disease specific features (captured in scoring systems such as the Dynamic International Prognostic Scoring System (DIPSS)[6] and Mutation-Enhanced International Prognostic Scoring System 70+ v2.0 (MIPSS70+ v2.0)[7].

Relapse post-allo-HCT remains a considerable challenge and no prognostic score accurately predicts the risk of relapse. Around 20-30% of patients will relapse within 3-years, most commonly within the first 12 months[5,9,10,11]. Post-allo-HCT strategies to reduce the risk of overt relapse include close monitoring of measurable residual disease (MRD), when a suitable mutation is present, and chimerism monitoring, to guide immunosuppression weaning and the use of pre-emptive adoptive

immunotherapy with donor lymphocyte infusions (DLI) if feasible and required. However, previous work from the Chronic Malignancies Working Party of the EBMT has demonstrated a marked variation in MRD and chimerism monitoring practice, with resultant heterogeneous approaches to the use of DLI following allo-HCT for MF[12]. Moreover, in case of frank relapse, therapeutic approaches vary widely from palliation and DLI to reintroduction of JAK inhibitors or even a second allo-HCT in selected individuals.

Although, DLI is widely used in the post-transplant setting for a range of disorders, optimal timing and dosing remains undetermined in MF allo-HCT patients. Practically, in this context, DLI can be considered as 'pre-emptive' when use is triggered by mixed donor chimerism or re-emergence of MRD in the absence of clear relapse and 'therapeutic' when there is evidence of clinician-defined relapse. DLI is most commonly delivered in an escalating dose regimen (EDR) or as 'bulk salvage' therapy, the selection of which is determined by disease relapse kinetics, type of donor, degree of T-cell depletion, physician choice and desired clinical endpoint.

To date, there is limited data on the efficacy of DLI following MF allo-HCT which has been evaluated in a small number of studies. A previous single centre case series (n=17) highlighted that pre-emptive DLI as an EDR for molecular relapse post MF allo-HCT (as evidenced by an increase of *JAK2* V617F allele burden determined by a highly sensitive quantitative PCR) led to molecular complete response in 8/8 patients, in comparison to 4/9 patients with clinical relapse achieving CR when DLI was used as a salvage treatment[13]. A further single centre study (n=27), published over a decade ago, reported a CR rate of 39% following DLI use for relapse, and an estimated OS of 70% when DLI was consolidated by a second allo-HCT[14].

Given the heterogeneous and retrospective nature of these studies and the absence of intention to treat analyses, outcomes for relapsing/frankly relapsed patients in the real world are unknown and are likely to be worse than those reported. Moreover, only a minority of relapsed MF patients will be fit enough to undergo a second allo-HCT procedure.

It is clear that additional data on the safety and efficacy of DLI use in MF allo-HCT setting is required to guide clinical decision making in this difficult patient group. We hereby report on a multicentre cohort of MF patients who received DLI post allo-HCT (n=28), aiming to describe the variation between centres regarding DLI use to summarise 'real world' safety and efficacy.

Methods: Patient selection included MF allo-HCT patients from 8 European transplant centres who received DLI between 2005-2022. Patients who received at least one dose of DLI were included. Data was retrospectively collected from 28 patients following systematic review of medical records. Patients who received DLI in addition to other salvage therapies were also included and details of these additional therapies are presented below. Patient demographics, disease and transplant characteristics data were collected. Pre-emptive DLI was utilised when there was a fall in chimerism or evidence of molecular relapse. The fall in chimerism that would trigger DLI use was dependant on each centre's experience and protocols. Chimerism measurements were performed on either CD34+ cells, T-cells, granulocytes or total cells depending on centre's practice. Evaluation of chimerism dynamics is considered only where there were paired measurements using the same method. Therapeutic DLI was used for clinician-defined relapse which included marrow assessment or relapse evaluated using clinical criteria (haematological, peripheral blood film findings, reoccurrence or progression of splenomegaly). No patients received prophylactic DLI. Response to DLI was assessed by International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) defined response criteria, albeit we acknowledge these are not validated in the post allo-HCT setting[15]. For toxicity assessment, we collected key outcomes: inpatient admissions and Grade 3–4 adverse events (AEs) as defined by the Common Terminology Criteria for Adverse Events (CTCAE) version 4·02 grading system. Data collection process was approved and registered at University College Hospital London for contributing centres. All data were anonymised at source and treated according to the principles of the Declaration of Helsinki and the UK Data Protection Act (1998). All

patients had been registered with the EBMT and consented for research as part of the consent process.

Statistical analysis

Overall survival (OS) censored at second allo-HCT and event-free survival (EFS) (events: first occurrence of progression/relapse or death in continued response) were estimated using the Kaplan-Meier method[16] and compared across groups with the log-rank test[17] and univariate Cox analysis[18]. Follow-up was estimated with the inverse Kaplan-Meier method[19]. To avoid severe bias possibly introduced by early deaths and/or short follow-up (less than 3 months after first infusion), landmark analysis was performed to examine effect of DLI plan (EDR vs. salvage) on EFS and OS. Competing risk analysis was used to estimate relapse and NRM incidence and cumulative incidence functions between groups were compared using Gray's test[20]. Time 'zero' was set at date of first DLI infusion for all survival outcomes. Because of the small number of events, multivariate analysis was not attempted for any of the outcomes. All analyses were performed for purely descriptive purposes and no adjustments for multiple testing were made to the alpha error level. Software employed was STATA (StataCorp. 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP) and EZR [21]

Results: Patient, disease and transplant characteristics are shown in **Table 1.** Median age was 58 years (IQR:53 – 62.5) and 19 (68%) were male. Driver mutation status was primarily *JAK2* V617F; n=18 (64.3%). A total of 16 patients (57.1%) received a JAK inhibitor prior to allo-HCT. At the time of allo-HCT, Karnofsky performance status (KPS)_was >80 in all patients and the majority had DIPSS+ Intermediate-2 (16/28; 57%) or high-risk disease (5/28; 18%). Splenomegaly, as determined by palpation or imaging, was present in 16/28 (57%) patients. Median time from diagnosis to allo-HCT was 23.4 months (IQR:8-44). Regarding donor type, 14 (50%) had a Matched Sibling Donor (MSD) and 14 (50%) an URD. The majority of patients received PBSC (n=26; 92.9%). *In vivo* T cell depletion was utilised in 20 (71.2%) cases, with 19/20 patients receiving anti-thymocyte globulin (ATG).

Regarding Graft versus Host Disease (GVHD) status prior to DLI, 11 (39%) patients had a history of acute and 8 (29%) patients had chronic GVHD, respectively. 1 patient in each group had severe grade (G3) GvHD with the rest having a lower grade (G1-2). Of note, 4 patients had active chronic GvHD at the time of DLI. Indication for DLI was recorded as either 'therapeutic' for haematological/ clinical relapse (n=13) or 'pre-emptive' (n=15), triggered by a decrease in recipient chimerism (n=13) or MRD (n=2) without overt relapse. The median chimerism for these patients that triggered the adoption of DLI was 61% recipient (IQR, 23 – 79). No clear features of haematological/clinical relapse was evident in any of the 15 patients included in this pre-emptive group as determined by the treating clinician. .

For the entire cohort, median time to DLI administration was 10.4 months (IQR:5.5-23.6 months). Median number of DLI doses administered was 2 (range, 1-5), with a median 1st dose of 1x10^6/kg (range 0.5 – 10). Of 16 patients receiving >1 dose of DLI, 12 were part of a planned escalated dose regimen. All such cases received at least 2 infusions. Median follow-up from 1st DLI was 55.4 months (IQR:27.7-96.5). Outcomes for both the pre-emptive and therapeutic DLI cohorts at the end of the follow up period are displayed in **Figure 1**. A total of 16/28 (57%) patients had an IWG-MRT defined response; CR (n=9, 4 were in CR pre-DLI), PR (n=1) and clinical improvement (n=6). Stable disease was reported in 5 patients with 7 patients showing no response or progression.

Regarding pre-emptive DLI use, for the 13 patients who received DLI for falling chimerism without evidence of overt/molecular relapse, 4 remained in CR, 1 achieved CR and 2 achieved clinical improvement. A total of 3 patients had stable disease, while 3 patients eventually showed progression. The two patients who received pre-emptive DLI for molecular response (n=2), achieved CR and PR respectively. Regarding therapeutic DLI use for clinician defined relapse, response was achieved in a total of 7/11 patients; CR (n=3), clinical improvement (n=4), stable disease (n=2), and progressive disease (n=4).

A total of 13 patients received additional treatment either before, during or after DLI administration. This can be summarised as follows; in the pre-emptive cohort 1 patient received a combination of a hypomethylating agent, lenalidomide and ruxolitnib, 2 patients received ruxolitinib only and 3 patients proceeded to a 2nd transplant post -DLI use. In the 'therapeutic' DLI cohort, patients received either intensive chemotherapy (n=2), venetoclax and azacytidine (n=2), ruxolitinib (n=2) and 1 patient had a second transplant post -DLI. The cohort number was too small for a sub-analysis of effect.

Chimerism levels, either PB or BM, improved in 16 patients (**Figure 2**) when measured prior to and post-DLI, with a median increase of 17% (IQR, 0 – 51%). Where DLI was administered for falling chimerism, this increased from a pre-DLI baseline in 9/13 patients following a median of 2 infusions (range, 1-4). A total of 5 patients remained in remission with a median follow up 55 months. For clinical relapse, 9/15 patients had a response and remained in remission (median follow up: 42 months).

Regarding complications in the post DLI period, DLI induced aGVHD was reported in 11 cases (39%), with grade 3-4 aGVHD in 5 (18%). Regarding donor effect on DLI induced GVHD, a total of 7/11 and 3/5 cases respectively had undergone an URD transplant. Overall, regarding additional toxicity occurring early after DLI administration, there was one grade 5 AE due to pneumonia complicated by Acute Respiratory Distress Syndrome (ARDS) on a background of grade 4 heart failure. There was 1 grade 4 neutropenia and thrombocytopenia reported and 1 grade 3 Alanine Transferase enzyme increase.

For the entire cohort, median OS from time of 1st DLI, censored at time of 2nd allo-HCT (n=4), was 62.6 months (IQR:10- NR)**.** OS estimates for both the pre-emptive and therapeutic cohorts are

displayed in **Figure 3.** Cumulative incidence of relapse/ progression after 1st DLI administration (death competing) was 30.8% (95% CI 14.4-48.9%) at 6-months. Regarding cause of death, this was predominantly due to either progressive disease (n=8/14) or infection (n=3/14). Other causes included graft failure (n=1) and secondary malignancy (n=1) whereas the cause was not documented for one case.

Univariate analysis identified older recipient age (>60 years) and high DIPSS+ score as significant factors for both EFS and OS after 1st DLI (p=0.02 and 0.03; p=0.02 and 0.02 respectively). Presence of the *ASXL1* mutation was significant for adverse EFS, but not OS, while peripheral or bone marrow blast count of >5% was only significant for OS (p= 0.0048) but not EFS (p =0.0632). Type of donor, T - cell depletion and disease status at the time of the transplant were not significant for either OS or EFS. The complete univariate analysis is presented in **Table 2.**

Next, we analysed outcomes following escalated dose regimen (EDR) use versus bulk salvage DLI use. An EDR was utilised in 12/28 patients (7 patients with either falling chimerism or molecular relapse and 5 with clinician defined relapse). From time of 1st DLI administration, EFS and OS were better in comparison to those receiving bulk salvage DLI (EFS hazard ratio (HR) 0.25 (95% CI 0.07-0.89), p=0.033; OS HR 0.28 (95%CI 0.08-1.01), p=0.052.) **(Figure S1 A+B).** Three-month landmark analysis of EFS and OS also suggested superior outcomes in the EDR group (borderline significance: EFS HR 0.31 (95% CI 0.08-1.17); OS HR 0.33 (95%CI 0.09-1.24)). The main reason behind more favourable EFS and OS of the EDR group appears to be a significantly lower incidence of relapse/progression (12.5% vs. 52% at 6 months post first infusion, Gray's p=0.038), whereas NRM incidence did not differ between the two groups (p=0.71) **(Table S1).**

Discussion

Despite increasing MF allo-HCT activity across Europe, there remains marked variation in MRD and chimerism monitoring and triggers for DLI utilisation[22,23]. Our current study highlights marked variation in practice among 8 large transplant centres in Europe. Here, triggers for DLI were either pre-emptive use due to decreases in donor chimerism/ molecular relapses or therapeutic use for clinician defined relapse. Despite the small numbers, heterogeneity and limitations inherent to such a retrospective study addressing a relatively rare situation, this study does highlight efficacy of DLI use in these settings. By applying IWG-MRT criteria to the MF post allo-HCT setting, response rates could be summarised as follows: with 14/28 (50%) being in remission or having stable disease at the end of the follow up period and 9/28 (32%) achieving CR post DLI. One patient with stable disease went on to have a second allo-HCT and remained in remission. Such results highlight the efficacy of DLI in this setting, but we must acknowledge that this was a heterogenous cohort, some of whom also received adjunctive therapies either pre- or post DLI including HMA or JAK inhibitors or even intensive chemotherapy.

Given the lack of alternative treatments at such a challenging cohort of patients, DLI offers a valid option for clinicians if the MRD kinetics are suggestive of imminent relapse or a drop in donor chimerism is detected and acted on in a timely manner. Most patients in this cohort, where samples were available for assessment, responded to DLI by demonstrating an increase in recipient chimerism. As expected, rates of DLI-induced GVHD were not insignificant, with 18% of the overall cohort experiencing grade 3 or 4 acute GVHD following the use of DLI, albeit we must acknowledge there was a range of conditioning regimens, T cell depletion strategies and donor types. Moreover, for the whole cohort, 11 patients had a history of aGVHD prior to DLI use; 6 of whom also had cGVHD, while 2 patients had a history of *de novo* cGVHD. Of note, no significant difference in OS was observed in the pre-emptive DLI cohort when compared to the therapeutic DLI cohort.

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The use of EDR DLI was associated with better outcomes when compared to bulk salvage DLI, accounted for by less relapse/ disease progression, but this finding is subject to several limitations and biases. Patients who received EDR had lower DIPSS+ scores and PB Blast >5% before transplantation compared to those who received no EDR. Moreover, EDR DLI was utilised in 7 patients with falling chimerism or molecular relapse and only 5 patients with clinician defined relapse .

Other limitations of this study include its retrospective nature and long duration of period covered (2005-2022). Additionally, the definitions for response were derived by IWG-MRT, but this was subject to a clinician's interpretation and the quality of patient notes that we systematically reviewed. There was heterogeneity in the donors, stage of disease at transplantation, and baseline characteristics. The rarity of the disease and its therapies in the post-transplant setting preclude a multivariate analysis, despite adequate follow-up. This is a selected cohort of MF patients post allo-HCT who have survived long enough (at least 3 months and many of them for many years, up to 16 years) to receive DLI, having overcome the risk of early death following allo-HCT. It is important to note that no data were collected for patients who underwent transplantation at participating centres during the same period but did not receive DLI for any reason (donor availability, patient suitability, GVHD, chimerism/relapse kinetics etc). Nonetheless, this study provides valuable insight into the realistic and clinically relevant outcomes of DLI administration in MF following allo-HCT across a number of large transplant centres over a period of 17 years.

Our study demonstrates that pre-emptive and therapeutic DLI can lead to favourable responses, including complete and partial remissions, as well as clinically relevant improvements. Pre-emptive strategies should be initiated at the time of detection of molecular relapse following immunosuppression wean or when a drop in donor chimerism is detected. Rates of success from available data as highlighted above suggest higher rates of success for molecular relapse rather than

haematological relapse as expected. There remains currently no established role for prophylactic DLI in MF allo-HCT. The small number of cases we collected likely highlights underutilisation of this important strategy and we think that more DLI use should be encouraged. One of the reasons behind this could be the lack of specific guidance or large randomized trials. Peer-reviewed guidelines to suggest triggers and approaches to DLI are still scarce[24]. Indeed, as can be seen from our data, heterogeneous approaches were taken, often centre dependent. Multicentre and prospective studies, ideally in the context of a randomized controlled trial, are required to help guide on the exact timing and regimen of DLI that will yield optimal results with the least toxicity and inform future guidelines.

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Conflicts of Interests

AR: Conference fees by Gilead

All other others declare no relevant conflicts of interests
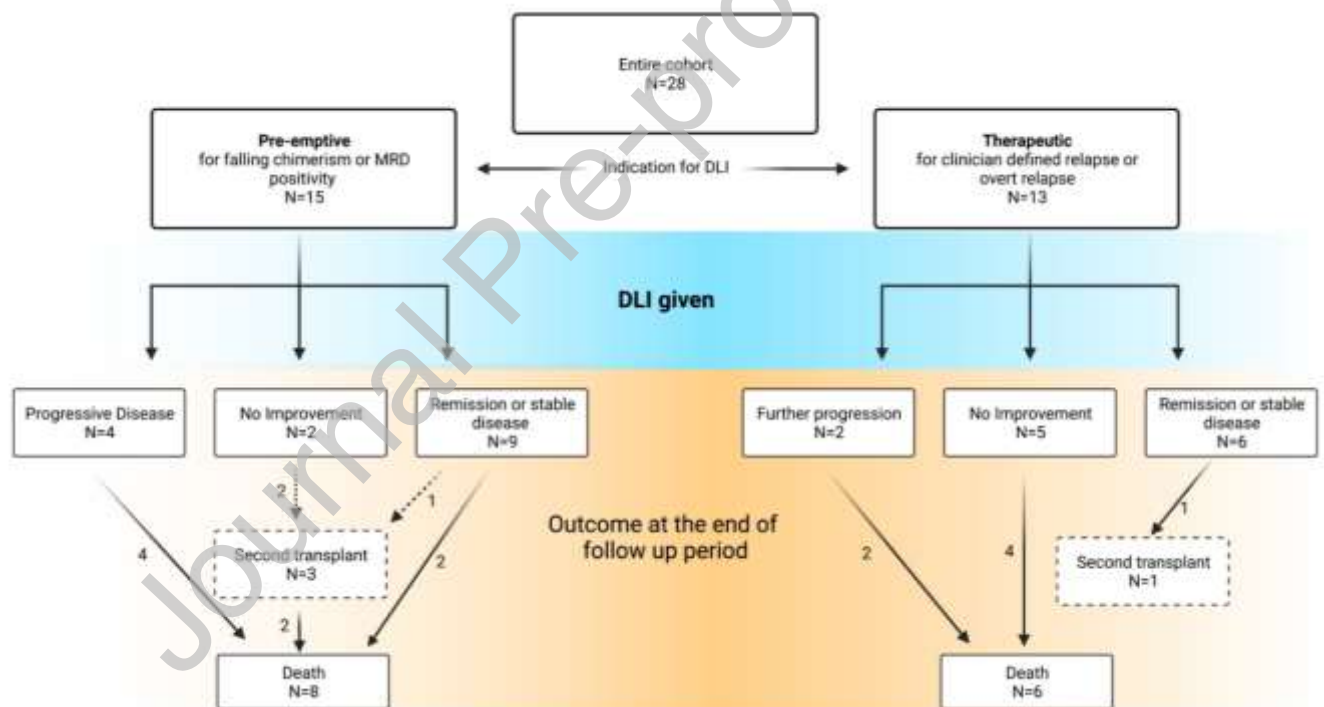
Figure 1. Outcomes at end of follow up period of patients who received pre-emptive or therapeutic Donor Lymphocyte Infusion (DLI). For patients who received pre-emptive DLI, if no increase in chimerism was achieved but without progressive disease, their outcome was regarded as 'no improvement'. For patients who have received therapeutic DLI, if they were already in PD, lack of response was defined as 'No improvement'.

Chimerism change

Figure 2: Recipient Chimerism dynamic changes between pre- and post- Donor Lymphocyte Infusion.

A total of 13 paired measurements were available. When more than one type of paired chimerism

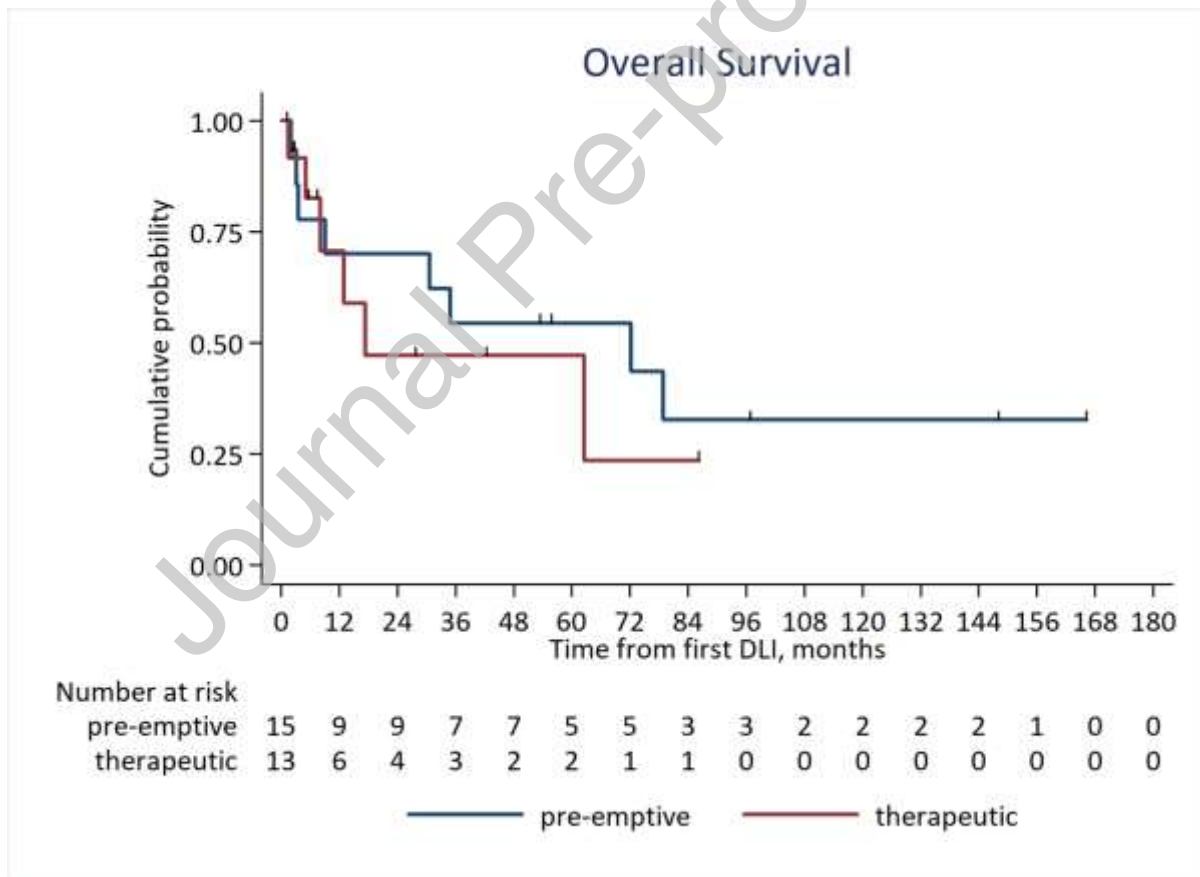measurement was available, we present CD34% over CD3% or total cells or other marker (e.g. CD15).

Figure 3: Kaplan-Meier curves for overall survival of patients treated with either pre-emptive DLI or

therapeutic DLI censored at time of second transplant where relevant (log-rank p=0.57).

Patient and Disease Characteristics (n=28)		
Age at time of DLI, years (IQR)		58 (52.5 – 62.75)
Sex, Male		19 (67.9%)
DIPSS- Plus score	Low	0/28
	Intermediate-1	6 (21.4%)
	Intermediate-2	16 (57.1%)
	High	5 (17.8%)
	Missing	1 (3.7%)
Splenomegaly	Yes	16 (57.1%)
	No	6 (21.4%)
	Not reported	6 (21.4%)
Mutational Status	*JAK2* V617F	18 (64.3%)
	CALR	2 (7.1%)
	MPL	0
	Triple negative	3 (10.7%)
	Unknown	5 (17.8%)
HCT-CI	0	13 (46.4%)
	1-2	7 (25%)
	≥3	8 (28.6%)
	Unknown	2 (7.14%)
KPS	100	8 (28.6%)
	90	9 (32.1%)
	80	10 (35.7%)
	Unknown	1 (3.5%)
Prior Exposure to JAK Inhibitors	Yes	16 (57.1%)
	No	12 (42.9%)
Transplant characteristics and outcomes		
Donor Type	Sibling	14 (50%)
	Matched unrelated 10/10	13 (46.5%)
	Mismatched unrelated 9/10	1 (3.5%)
T-cell depletion	Yes	20 (71.4%)
	No	5 (17.8%)
	Not known	3 (10.7%)
Stem Cell source	Peripheral Blood Stem Cells	26 (92.9%)
	Bone marrow	2(7.1%)
Donor's sex	Male	18 (64.3%)
	Female	10 (35.7%)
Time to neutrophil engraftment, days (IQR)		20 (15-21)
Acute GvHD history prior to DLI	Yes	11 (39.3%)
	No	17 (60.7%)
Chronic GvHD	Yes	8 (28.6%)

history prior to DLI	No	20 (71.4%)

Table 1. Baseline Patient and Transplant characteristics and outcomes of the entire cohort. DLI donor Lymphocyte Infusion, DIPSS=Dynamic International Prognostic Scoring System, IQR= Interquartile range, HCT-CI= Haematopoietic Cell Transplantation specific Comorbidity Index, KPS= Karnofsky Performance Scale, JAK= Janus Kinase, GvHD= Graft versus Host Disease.

Patient or Transplant Variable		Number reported (%)	EFS (p value)	OS (p value)
Age >60	Y	9/28 (32%)	0.0183	0.0041
	N	19/28 (68%)		
DIPSS+	High Risk	5/28 (18%)	0.0199	0.0236
	All other Risk	21/28 (82%)		
HCT-CI > 0	Y	14/26 (53.8%)	0.0694	0.2899
*2 unknown	N	12/26 (46.2%)		
A*SXL1* mutation	Y	3/28 (11%)	0.0389	0.1519
	N	15/28 (89%)		
PB blast >5%	Y	6/28 (21.4%)	0.0632	0.2454
	N	22/28 (78.6%)		
Hb <100g/L (*2 unknown)	Y	10/26 (38.5%)	0.0176	0.1023
	N	16/26 (61.5%)		
KPS < 90 (*1 unknown)	Y	10/27 (37%)	NS	0.3048
	N	17/27 (63%)		
PD at time of transplant	Y	10/24 (41.6%)	NS	
(*3 unknown)	N	14/24 (58.4%)		0.0990
Unrelated donors vs Sibling donor	Y	14/28 (50%)	NS	
	N	14/28 (50%)		0.4982
Evidence of GVHD before DLI	Y	8/28 (28.6%)	NS	0.3609
	N	20/28 (71.4%)		
Clinical relapse at time of DLI	Y	15/28 (53.6%)	NS	0.6613
	N	13/28 (46.4%)		
Time to first DLI <6 months	Y	8/28 (28.6%)	NS	
	N	20/28 (71.4%)		0.3268
Donor CMV positive status	Y	13/28 (46.4%)	NS	0.3486
	N	15/28 (53.6%)		
Recipient CMV positive status	Y	16/28 (57.1%)	NS	0.4885
	N	12/28 (42.9%)		
T-cell depletion in conditioning	Y	21/26 (80.8%)	NS	0.2107
*2 unknown	N	5/26 (19.2%)		
BM blast>5% (*10 unknown)	Y	3/18 (16.7%)	NS	NS
	N	15/18 (83.3%)		

Table 2. Univariate Cox analysis including disease and transplant related factors and effect on both event free survival (EFS) and overall survival (OS) post DLI administration. DLI donor Lymphocyte Infusion, DIPSS= Dynamic International Prognostic Scoring System, PB= Peripheral Blood, Hb =Haemoglobin, KPS= Karnofsky Performance Scale, PD=progressive disease, GVHD= Graft versus Host Diseasem, CMV=Cytomegalovirus, BM=Bone Marrow, NS= Not significant.