Early administration of donor lymphocyte infusions upon molecular relapse after allogeneic hematopoietic stem cell transplantation for chronic myeloid leukemia: a study by the Chronic Malignancies Working Party of the EBMT

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Supplementary material

Supplementary methods

Centers report minimum essential data (MED-A) to a central database for all transplants performed. Many centers also report a more comprehensive dataset (MED-B). Informed consent was obtained locally according to the regulations applicable at the time of transplant. Since January 1st 2003 the EBMT has required centers to confirm that written informed consent has been obtained prior to data acceptance. Special DLI forms (MED-C) were sent to all EBMT centers reporting patients who had received DLI for CML relapse. The total sample included 1045 patients from 138 EBMT centers and 31 centers participated in this study. A total of 344 DLI forms were received. Each participating center completed the questionnaire for all consecutive patients eligible for the study in their institution while non-participating centers reported none. Patients whose relapse was first detected in cytogenetic, hematologic or advanced phase (156 patients), or who had this information missing (33), were not included in the study. We thus selected for the study 155 patients diagnosed with molecular relapse and with complete data for the analysis, from 28 EBMT centers. Each participating center completed the questionnaire for all consecutive patients eligible for the study in their institution.

Outcomes.

Acute and chronic GvHD occurring after DLI were reported and graded according to the standard clinical criteria (modified Glucksberg criteria for acute GvHD and chronic GvHD as defined by Shulman et al).[16-18] Centers reported GvHD as being acute or chronic according to the initial clinical presentation. As late onset acute GvHD was not defined at the

time when most of these patients were treated we pooled acute and chronic GvHD occurring after DLI for cumulative incidence.

Statistical analysis

Cox regression models of DLI-related mortality and survival were built entering covariates associated ($p \leq 0.1$) with outcome in univariate analysis. The following covariates were evaluated for their association with DLI-related mortality and survival post-DLI: initial cell dose (ICD), source of stem cell, center, prior T-cell depletion for GvHD prophylaxis for stem cell transplantation, disease stage at DLI, donor recipient sex combination, age at transplant, time from molecular relapse to DLI, donor type, GvHD prior to relapse. For the final Cox regression model the following variables were kept: donor type, time from molecular relapse to DLI and disease stage at DLI. All p values are nominal values.

Supplementary Table S1

Characteristics of patients receiving DLI for CML molecular relapse

N	**155**
Patient sex (m/f)	82 (53%)/73 (47%)
Median age in years	34 (4-64)
Year of transplant	1997 (1983-2003)
Donor siblings/unrelated	84 (54%)/71 (46%)
Bone marrow/PB/missing	129 (83%)/25 (16%)/1 (1%)
T-cell depletion no/yes	56 (36%)/99 (64%)
Acute GvHD post-transplantation	95 (61%)
Grade I	50 (53%)
Grade II-IV	45 (47%)
Unknown	9 (6%)
Chronic GvHD post-transplantation	74 (48%)
Limited	43 (58%)
Extensive	31 (42%)
Unknown	15 (10%)
Interval relapse-DLI	
< 6 months	64 (41%)
≥ 6 months	88 (57%)
Unknown	3 (2%)
Stage of disease at time of DLI	
Molecular relapse	85 (55%)
Cytogenetic relapse	37 (24%)
Hematologic relapse	25 (16%)
Accelerated phase	6 (4%)
Blastic phase	2 (1%)

Reason for DLI	
Planned	2 (1.3%)
Insufficient response	1 (0.7%)
Progressive disease (Mol:42,Cy:37,CP:25, Ad:8)	96 (61.9%)
Relapse (molecular)	55 (35.5%)
Not specified	1 (0.6%)
GvHD present at DLI	
No	111 (72%)
Yes	13 (8%)
Unknown	31 (20%)
Number of DLI	
1	83 (54%)
2	25 (16%)
≥3	47 (30%)
Year when DLI given	
1990-1997	41 (26.5%)
1998-2004	114 (73.5%)
Cell dose (1st DLI)	
$\leq 1.0x10^6$ $CD3^+$/kg	44 (28%)
$>1.0x10^6 \leq 1x10^7$ $CD3^+$/kg	58 (37%)
$>1.0x10^7 \leq 1x10^8$ $CD3^+$/kg	20 (13%)
$>1.0x10^8$ $CD3^+$/kg	5 (3%)
Unknown	28 (18%)

DLI: donor lymphocyte infusion, m: male, f: female, PB: peripheral blood, GvHD: graft versus host disease, Mol: molecular, Cy: cytogenetic, CP: chronic phase, Ad:advanced disease