

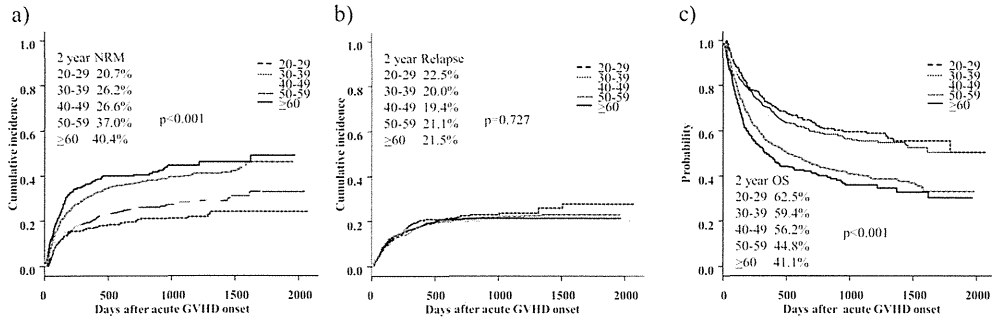
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### Figure Legends

- a) Cumulative incidence of non-relapse mortality for the patients in each age group (20–29, 30–39, 40–49, 50–59,  $\geq 60$  years) with grade II–IV acute GVHD
  
- b) Cumulative incidence of relapse for the patients in each age group (20–29, 30–39, 40–49, 50–59,  $\geq 60$  years) with grade II–IV acute GVHD
  
- c) Overall survival for the patients in each age group (20–29, 30–39, 40–49, 50–59,  $\geq 60$  years) with grade II–IV acute GVHD

# Leukemia and Lymphoma



252x84mm (150 x 150 DPI)

## Leukemia and Lymphoma

**Table I Patient characteristics**

Age groups	20-29	30-39	40-49	50-59	≥60	p
Number of patients	318	514	636	835	379	
Sex						0.49
Male	184 (58%)	293 (57%)	378 (59%)	499 (60%)	238 (63%)	
Female	134 (42%)	221 (43%)	258 (41%)	336 (40%)	141 (37%)	
Performance status						0.03
0-1	270 (85%)	461 (90%)	553 (87%)	712 (85%)	306 (81%)	
2-4	22 (7%)	24 (5%)	46 (7%)	65 (8%)	36 (9%)	
N.A.	26 (8%)	29 (6%)	37 (6%)	58 (7%)	37 (10%)	
Disease						<0.001
Acute myeloid leukemia	128 (40%)	223 (43%)	277 (44%)	343 (41%)	210 (55%)	
Acute lymphoblastic leukemia	114 (36%)	134 (26%)	128 (20%)	111 (13%)	42 (11%)	
Myelodysplastic syndrome	22 (7%)	50 (10%)	67 (11%)	126 (15%)	52 (14%)	
Myeloproliferative neoplasm	0 (0%)	5 (1%)	13 (2%)	13 (2%)	10 (3%)	
Chronic myeloid leukemia	13 (4%)	34 (7%)	18 (3%)	27 (3%)	6 (2%)	
Lymphoma	35 (11%)	64 (12%)	119 (19%)	191 (23%)	54 (14%)	
Plasma cell neoplasm	0 (0%)	2 (0%)	3 (0%)	9 (1%)	0 (0%)	
Other leukemia	1 (0%)	2 (0%)	4 (1%)	6 (1%)	1 (0%)	
Disease status						<0.001
Standard	168 (53%)	289 (56%)	325 (51%)	382 (46%)	140 (37%)	
Advanced	144 (45%)	222 (43%)	297 (47%)	434 (52%)	225 (59%)	
N.A.	6 (2%)	3 (1%)	14 (2%)	19 (2%)	14 (4%)	
Sex mismatch						<0.001
Match	141 (44%)	275 (54%)	333 (52%)	419 (50%)	175 (46%)	
Male donor to female recipient	78 (25%)	126 (25%)	149 (23%)	200 (31%)	79 (21%)	
Female donor to male recipient	83 (26%)	97 (19%)	127 (20%)	179 (28%)	88 (23%)	
N.A.	16 (5%)	16 (3%)	27 (4%)	37 (6%)	37 (10%)	
CMV serostatus (donor/recipient)						<0.001
Positive/ positive	117 (37%)	228 (44%)	304 (48%)	423 (51%)	151 (40%)	
Negative/ positive	74 (23%)	113 (22%)	131 (21%)	212 (25%)	106 (28%)	
Positive/ negative	25 (8%)	41 (8%)	30 (5%)	31 (4%)	12 (3%)	
Negative/ negative	41 (13%)	47 (9%)	54 (8%)	52 (6%)	49 (13%)	
N.A.	61 (19%)	85 (17%)	117 (18%)	117 (14%)	61 (16%)	
Donor						<0.001

## Leukemia and Lymphoma

Matched related	66 (21%)	120 (23%)	174 (27%)	211 (25%)	56 (15%)	
Mismatched related	31 (10%)	49 (10%)	42 (7%)	69 (8%)	32 (8%)	
Matched unrelated volunteer	88 (28%)	139 (27%)	169 (27%)	215 (26%)	104 (27%)	
Mismatched unrelated volunteer	59 (19%)	114 (22%)	129 (20%)	159 (19%)	53 (14%)	
Cord blood	71 (22%)	82 (16%)	114 (18%)	166 (20%)	133 (35%)	
N.A.	3 (1%)	10 (2%)	8 (1%)	15 (2%)	1 (0%)	
Conditioning regimen						<0.001
Myeloablative conditioning	287 (90%)	456 (89%)	525 (83%)	387 (46%)	80 (21%)	
Reduced intensity conditioning	30 (9%)	55 (11%)	106 (17%)	441 (53%)	297 (78%)	
N.A.	1 (0%)	3 (1%)	5 (1%)	7 (1%)	2 (1%)	
GVHD prophylaxis-1						0.001
<b>Cyclosporine</b> -based	150 (47%)	245 (48%)	312 (49%)	357 (43%)	133 (35%)	
Tacrolimus-based	162 (51%)	257 (50%)	319 (50%)	464 (56%)	238 (63%)	
Other	6 (2%)	12 (2%)	6 (1%)	14 (2%)	8 (2%)	
GVHD prophylaxis-2						<0.001
With methotrexate	281 (88%)	453 (88%)	568 (89%)	678 (81%)	248 (65%)	
Without methotrexate	37 (12%)	61 (12%)	68 (11%)	157 (19%)	131 (35%)	
GVHD prophylaxis-3						0.08
Without in-vivo T cell depletion	310 (97%)	505 (98%)	624 (98%)	809 (97%)	362 (96%)	
With in-vivo T cell depletion	8 (3%)	9 (2%)	12 (2%)	26 (3%)	17 (4%)	
Acute GVHD grade						0.63
II	210 (66%)	351 (68%)	418 (66%)	543 (65%)	243 (64%)	
III	78 (25%)	110 (21%)	163 (26%)	211 (25%)	105 (28%)	
IV	30 (9%)	53 (10%)	55 (9%)	81 (10%)	31 (8%)	
Median onset days of acute GVHD	21	19	22	23	23	<0.001
(range)	(5-92)	(4-89)	(1-130)	(3-124)	(3-108)	
Initial organ involvement						
Liver						0.88
+	24 (8%)	36 (7%)	49 (8%)	65 (8%)	31 (8%)	
-	293 (92%)	476 (93%)	585 (92%)	763 (91%)	347 (92%)	
N.A.	1 (0%)	2 (0%)	2 (0%)	7 (1%)	1 (0%)	
Gut						0.30
+	91 (29%)	162 (32%)	197 (31%)	281 (34%)	127 (34%)	
-	227 (71%)	351 (68%)	438 (69%)	548 (66%)	251 (66%)	
N.A.	0 (0%)	1 (0%)	1 (0%)	6 (1%)	1 (0%)	
Skin						0.004

## Leukemia and Lymphoma

+	268 (84%)	429 (83%)	517 (81%)	654 (78%)	287 (76%)
-	50 (16%)	82 (16%)	119 (19%)	173 (21%)	91 (24%)
N.A.	0 (0%)	3 (1%)	0 (0%)	8 (1%)	1 (0%)

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N.A., not available; CMV, cytomegalovirus; GVHD, graft-versus-host disease

**Table II Effect of age on outcome after grade II–IV acute GVHD adjusted by multivariate analysis\***

Age group	Non-relapse mortality		Relapse		Overall survival	
	Hazard ratio	<i>p</i>	Hazard ratio	<i>p</i>	Hazard ratio	<i>p</i>
20-29	Reference		Reference		Reference	
30-39	1.2 (0.9-1.7)	0.15	0.8 (0.6-1.2)	0.29	1.1 (0.9-1.4)	0.27
40-49	1.3 (0.98-1.8)	0.07	0.8 (0.6-1.1)	0.22	1.3 (1.02-1.6)	0.03
50-59	1.9 (1.4-2.5)	<0.001	0.9 (0.7-1.2)	0.48	1.9 (1.5-2.4)	<0.001
≥60	2.0 (1.5-2.7)	<0.001	0.9 (0.6-1.2)	0.42	2.3 (1.8-3.0)	<0.001

GVHD, graft-versus-host disease

\*The effect of each age group on overall survival, non-relapse mortality, and relapse was adjusted for the following factors: patient gender, performance status, disease, disease status, sex mismatch between recipient and donor, cytomegalovirus serostatus, donor source, conditioning regimen, GVHD prophylaxis, acute GVHD grade, day of onset of acute GVHD, and initial organ involvement.



**Table III Effect of older age on non-relapse mortality in grade II and III-IV groups adjusted by multivariate analysis\***

Age group	Acute GVHD grade			
	Grade II		Grade III-IV	
	Hazard ratio	<i>p</i>	Hazard ratio	<i>p</i>
20-29	Reference		Reference	
30-39	1.8 (1.1-3.1)	0.03	1.0 (0.7-1.5)	0.82
40-49	1.6 (0.98-2.8)	0.06	1.2 (0.8-1.7)	0.35
50-59	2.9 (1.8-4.8)	<0.001	1.5 (1.03-2.1)	0.03
≥60	3.3 (1.9-5.7)	<0.001	1.5 (1.02-2.3)	0.04

GVHD, graft-versus-host disease

\*The effect of each age group on non-relapse mortality was adjusted for the following factors: patient gender, performance status, disease, disease status, sex mismatch between recipient and donor, cytomegalovirus serostatus, donor source, conditioning regimen, GVHD prophylaxis, day of onset of acute GVHD, and initial organ involvement.

**Table IV Primary, non-relapse causes of death in patients with grade II and III–IV acute GVHD**

Acute GVHD grade	Grade II		Grade III–IV	
	20–49	≥50	20–49	≥50
Age group				
Number of NRM	154	218	234	267
<b>Cause of non-relapse mortality, n (%)</b>				
Infection	45 (29.2%)	80 (36.7%)	72 (30.8%)	79 (29.6%)
Acute/chronic GVHD	6/14 (13.0%)	5/17 (10.1%)	51/7 (24.8%)	77/7 (31.5%)
Organ failure	25 (16.2%)	30 (13.8%)	34 (14.5%)	28 (10.5%)
Non-infectious pulmonary complication/ARDS	12/4 (10.4%)	18/8 (11.9%)	7/4 (4.7%)	14/9 (8.6%)
Hemorrhage	13 (8.4%)	15 (6.9%)	17 (7.3%)	12 (4.5%)
TA-TMA/SOS	11/2 (8.4%)	10/3 (6.0%)	16/5 (9.0%)	24/3 (10.1%)
Rejection/graft failure	2 (1.3%)	4 (1.8%)	2 (0.9%)	2 (0.7%)
Secondary malignancy	1 (0.6%)	8 (3.7%)	1 (0.4%)	0 (0%)
Other	14 (9.1%)	17 (7.8%)	18 (7.7%)	9 (3.4%)
Unknown	5 (3.2%)	3 (1.4%)	0 (0%)	3 (1.1%)
<i>p</i> value*	0.43		0.06	

GVHD, graft-versus-host disease; NRM, non-relapse mortality; ARDS, acute respiratory distress syndrome; TA-TMA, Transplant-associated thrombotic microangiopathy; SOS, sinusoidal obstruction syndrome

\* The chi-square test was used for overall comparison between the age groups in patients with grade II or III–IV acute GVHD.

