MUD SCT

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Outlines

- Optimal match criteria for unrelated adult donors
- Role of ATG in MUD-SCT
- Post-transplant cyclophosphamide for GVHD prophylaxis in MUD/MMUD patients

Related haploidentical donors are a better choice than matched unrelated donors: Point Ephraim Joseph Fuchs Logistical comparison of related haplo vs HLA-matched unrelated donors

	MUD	**Haplo**
Donor availability	20%-80%[18]	>95%
Time to graft acquisition	Slower	Faster
Time between collection and infusion	Longer	Shorter
Ease of repeat donations	Harder	Easier
Cost	Higher	Lower

Factors affecting outcomes of Allo-HSCT

- Pre-transplantation factors
  - Donor-recipient HLA matching
  - Graft cell-dose
  - Performance score and co-morbidity
  - Disease and disease status

  Conditioning and GVHD prophylaxis regimens

- Post-transplantation factors
  - Acute and chronic GVHD
  - Infections
  - Recurrent and second malignant neoplasms

What are the optimal match criteria for unrelated adult donors

- **NMDP/CIBMTR study (Lee et al; 3857 transplantation: 94% BM: 1988-2003)**
- High-resolution matching for HLA-A, -B, -C, and -DRB1 maximizes posttransplantation survival
- The study suggested that mismatches at HLA-B and -C may be less detrimental than those at HLA-A and -DRB1
- Survival was not affected by mismatching at either HLA-DQ or -DP
- HLA-C antigen mismatching conferred the greatest risk for mortality, grade 3 or 4 acute GVHD and chronic GVHD. a marrow graft would be better tolerated than PBSCs

Single locus mismatches at HLA-A, -B, -C, and -DRB1

	Survival			Disease-free survival			Treatment-related mortality			Acute graft-versus-host disease		
Factor	RR	95% CI	*P*	RR	95% CI	*P*	RR	95% CI	*P*	RR	95% CI	*P*
Any single locus (n = 985) vs matched (n = 1840)	1.25	1.13-1.38	<.001	1.23	1.12-1.36	<.001	1.40	1.25-1.56	<.001	1.48	1.29-1.68	<.001
Any single allele (n = 412) vs matched	1.30	1.14-1.46	<.001	1.28	1.13-1.46	.002	1.40	1.20-1.63	<.001	1.34	1.12-1.61	.002
Any single antigen (n = 573) vs matched	1.22	1.08-1.37	.001	1.20	1.07-1.35	.002	1.40	1.22-1.60	<.001	1.59	1.35-1.86	<.001
Any single allele vs any single antigen	1.07	0.92-1.24	.40	1.07	0.92-1.24	.39	1.00	0.83-1.19	.98	0.85	0.68-1.04	.12

Single locus mismatches at HLA-A, -B, -C, and -DRB1

		Survival			Disease-free survival			Treatment-related mortality			Acute graft-versus-host disease		
	n*	RR	95% CI	P	RR	95% CI	P	RR	95% CI	P	RR	95% CI	P
Matched	1840	1.00	—	—	1.00	—	—	1.00	—	—	1.00	—	—
HLA-A													
Allele	113	1.50	1.20-1.88	<.001	1.46	1.71-1.82	.001	1.65	1.24-2.10	<.001	1.62	1.19-2.20	.002
Antigen	161	1.24	1.02-1.52	.03	1.27	1.05-1.55	.02	1.39	1.10-1.77	.006	1.54	1.18-2.03	.002
Allele vs antigen	—	0.83	0.62-1.10	.19	0.87	0.65-1.15	.34	0.86	0.62-1.21	.39	0.95	0.64-1.41	.81
HLA-B													
Allele	99	1.25	0.97-1.60	.09	1.18	0.92-1.51	.20	1.41	1.06-1.87	.02	1.63	1.19-2.23	.002
Antigen	17	0.78	0.42-1.45	.43	0.72	0.38-1.34	.29	1.01	0.52-1.96	.97	1.60	0.79-3.21	.19
Allele vs antigen	—	0.62	0.32-1.21	.17	0.61	0.31-1.18	.14	0.72	0.35-1.46	.36	0.98	0.46-2.08	.96
HLA-C													
Allele	96	1.03	0.79-1.34	.84	1.11	0.86-1.42	.43	1.05	0.77-1.44	.76	0.98	0.68-1.40	.9
Antigen	382	1.22	1.06-1.39	.004	1.19	1.04-1.36	.009	1.40	1.20-1.64	<.001	1.60	1.33-1.93	<.001
Allele vs antigen	—	1.18	0.89-1.57	.24	1.08	0.82-1.41	.59	1.33	0.95-1.87	.09	1.63	1.11-2.42	.01
HLA-DRB1													
Allele	104	1.42	1.13-1.80	.003	1.39	1.10-1.75	.005	1.52	1.16-4.48	.002	1.20	0.83-1.73	.32
Antigen	13	1.81	0.96-3.41	.07	1.65	0.85-3.10	.12	2.29	1.17-4.48	.02	1.77	0.83-3.78	.1
Allele vs antigen	—	1.27	0.64-2.48	.49	1.19	0.61-2.31	.62	1.50	0.72-3.08	.26	1.46	0.64-3.37	.36

Do HLA matching requirements differ in selection of adult peripheral blood stem cell donors?

NMDP/CIBMTR analysis of HLA matching in 1933 unrelated PBSC transplantations

	N	RR	95% CI	p value
Mortality				
8/8 match	1243	1.00		
A allele MM	51	1.16	0.80-1.67	0.43
A antigen MM	85	1.17	0.88-1.55	0.29
A allele or antigen MM*	136	1.17	0.93-1.47	0.19
B allele MM	57	1.29	0.92-1.82	0.14
B antigen MM	16	1.01	0.50-2.04	0.97
B allele or antigen MM*	73	1.22	0.90-1.67	0.19
C allele MM	61	0.82	0.57-1.19	0.30
C antigen MM	189	1.41	1.16-1.70	0.0005
DRB1 MM	39	1.30	0.87-1.94	0.20

No significant effect was observed when the mismatch was at the allele-level only

The adverse effect of mismatching at the HLA-C locus was significant for recipients

In HLA-C mismatch: marrow graft would be better tolerated than PBSCs

Impact of specific HLA locus or allele mismatches as reported in recent (2013-2016) multicenter studies of unrelated HSCT

Ref.	N. of patients	Main conclusions	
5	2,646	Single HLA-A,B,C,DRB1 MM (either antigen or allele) associated with increased mortality, additional risk with <9/10 matched (including DQB1) donors	PBSC: 87%
13	8,539	Non-permissive DPB1 MM associated with increased mortality in 9-10/10 matched HSCT	
30	3,853	In 7/8 matched HSCT : >2 MM at DRB3/4/5, DQB1 or DPB1 loci associated with lower survival	PBSC: 85%
29	7,349	C*03:03/03:04 MM better tolerated, lower impact of C-locus MM explained by the high frequency of C*03:03/03:04 MM in the 7/8 matched group	BM: 60% PBSC: 40%
12	8,003	Single HLA-A,B,C,DRB1 MM associated with increased mortality, DQB1 MM associated with increased acute GVHD, non-permissive DPB1 MM associated with increased mortality in 10/10 or 8/8 matched cases	BM: 40% PBSC: 60%
15	7,898	Single HLA-A,B,C and double HLA-DRB1-DQB1 MM associated with increased mortality, HLA-A,B,C,DPB1 MM associated with higher risk of acute GVHD, reduced relapse only with C,DPB1 MM	
30	2,588	Reduced intensity conditioning HSCT: increased mortality in 7/8 matched HSCT, no impact of C*03:03/03:04 or permissive DPB1 MM	PBSC: 85%
16	803	Single HLA-A,B,C MM (9/10) associated with higher mortality, HLA-DRB1/DQB1 MM more permissive (high ratio of DRB1*11:01/11:04 and DQB1*03:01/03:02 MM)	PBSC: 77%
50	2,029	In 11/12 matched HSCT: single nucleotide polymorphism in the regulatory region of DPB1 locus associated with acute GVHD	
44	6,967	Patient and/or donor B*51:01 and patient C*14:02 associated with increased acute GVHD and mortality	
16	11,039	Donor age (>32 years) and 7/8, 6/8 mismatched donors associated with lower overall survival	

Role of ATG in MUD-SCT

Outcomes after matched unrelated donor versus identical sibling hematopoietic cell transplantation in adults with AML: CIBMTR 2002-2006; Saber et al, Blood 2012

Variable	MRD	8/8 MUD	7/8 MUD	P*
Size, n	624	1193	406	
Centers, n	62	99	84	
Median age, y (range)	52 (21-76)	51 (21-75)	48 (21-75)	< .001‡
Age group, y, n (%)				< .001
20-29	54 (9)	146 (12)	67 (17)	
30-39	74 (12)	142 (12)	70 (17)	
40-49	165 (26)	308 (26)	93 (23)	
50-59	229 (37)	372 (31)	113 (28)	
≥ 60	102 (16)	225 (19)	63 (16)	
Sex, n (%)				.04
Male	356 (57)	618 (52)	226 (56)	
Female	265 (42)	574 (48)	180 (44)	
Missing	3 (< 1)	1 (< 1)	0	
KPS, n (%)				< .001
≥ 90	382 (61)	700 (59)	231 (57)	
< 90	214 (34)	336 (28)	129 (32)	
Missing	28 (4)	157 (13)	46 (11)	
Race, n (%)				< .001
White	528 (85)	1134 (95)	359 (88)	
Black	38 (6)	21 (2)	27 (7)	
Asian	18 (3)	12 (1)	5 (1)	
Other—American Indian/Native Hawaiian	23 (4)	6 (1)	4 (1)	
Missing	17 (3)	20 (2)	11 (3)	
AML disease status at transplantation, n (%)				< .001
Primary induction failure	91 (15)	204 (17)	65 (16)	
CR1	337 (54)	547 (46)	150 (37)	
CR2	97 (16)	261 (22)	109 (27)	
First relapse	80 (13)	173 (15)	79 (19)	
Missing	19 (3)	8 (1)	3 (1)	

Outcomes after matched unrelated donor versus identical sibling hematopoietic cell transplantation in adults with AML: CIBMTR 2002-2006; Saber et al, Blood 2012

Conditioning regimen intensity, n (%)				
Traditional ablative	335 (54)	547 (46)	220 (54)	
Reduced intensity	135 (22)	336 (28)	104 (26)	
Nonmyeloablative	74 (12)	148 (12)	36 (9)	
Nontraditional ablative†	80 (13)	162 (14)	45 (11)	
Missing	0	0	1 (< 1)	.003
Stem cell source, n (%)				
BM	48 (8)	328 (27)	105 (26)	
Peripheral blood	576 (92)	865 (73)	301 (74)	< .001
GVHD prophylaxis, n (%)				
Missing	3 (< 1)	0	0	
None	14 (2)	8 (1)	4 (1)	
FK506 + MTX + other	241 (39)	578 (48)	191 (47)	
FK506 + other	104 (17)	249 (21)	79 (19)	
CsA + MTX + other	124 (20)	192 (16)	87 (21)	
CsA + other	125 (20)	149 (12)	39 (10)	
Other	13 (2)	17 (1)	6 (1)	< .001
Antithymocyte globulin, n (%)				
No	565 (91)	894 (75)	306 (75)	
Yes	59 (9)	299 (25)	100 (25)	< .001
Year of transplantation, n (%)				
2002	99 (16)	124 (10)	38 (9)	
2003	89 (14)	166 (14)	69 (17)	
2004	141 (23)	275 (23)	89 (22)	
2005	157 (25)	295 (25)	106 (26)	
2006	138 (22)	333 (28)	104 (26)	
Median follow-up of survivors, mo (range)	57 (2-97)	42 (6-89)	45 (3-85)	
Total deaths, n	397	624	773	1193	275	406

Outcomes after matched unrelated donor versus identical sibling hematopoietic cell transplantation in adults with AML: CIBMTR 2002-2006; Saber et al, Blood 2012

	n	MRD probability, % (95% CI)	n	8/8 MUD probability, % (95% CI)	n	7/8 MUD probability, % (95% CI)	P*	8/8 MUD vs MRD, P†	7/8 MUD vs MRD, P†	7/8 MUD vs 8/8 MUD, P†
ANC recovery	621		1192		406					
@ 28 d		96 (94-97)		93 (92-95)		92 (89-95)	.01	.008	.02	.59
@ 100 d		97 (96-99)		96 (94-97)		95 (93-97)	.03	.02	.04	.65
Platelet recovery	615		1183		398					
@ 60 d		87 (85-90)		83 (81-86)		81 (78-85)	.02	.02	.01	.40
@ 100 d		89 (86-91)		85 (83-87)		85 (81-88)	.05	.02	.05	.76
Acute GVHD grade B-D	622		1192		406					
@ 100 d		33 (29-36)		51 (48-54)		53 (48-58)	< .001	< .001	< .001	.51
Acute GVHD grade C-D	623		1193		406					
@ 100 d		12 (10-15)		25 (23-28)		31 (27-36)	< .001	< .001	< .001	.01
Chronic GVHD	608		1150		394					
@ 1 y		39 (35-43)		45 (42-48)		43 (38-48)	.03	.008	.19	.40
@ 3 y		44 (40-48)		48 (45-51)		46 (41-51)	.29	.11	.43	.63
TRM	604		1157		395					
@ 1 y		18 (15-21)		21 (19-23)		32 (27-37)	< .001	.08	< .001	< .001
@ 3 y		25 (22-29)		28 (25-31)		36 (32-41)	.001	.23	< .001	.001
Relapse	604		1157		395					
@ 1 y		32 (29-36)		35 (32-37)		27 (23-32)	.02	.34	.09	.005
@ 3 y		39 (35-43)		38 (35-41)		32 (28-37)	.06	.65	.02	.04
LFS	604		1157		395		.09‡			
@ 1 y		50 (45-54)		44 (41-47)		40 (36-45)	.013	.02	.004	.22
@ 3 y		35 (31-39)		34 (31-36)		31 (26-35)	.37	.46	.16	.35
Survival	624		1193		406		.01‡			
@ 1 y		55 (51-59)		52 (50-55)		45 (40-50)	.004	.28	.001	.008
@ 3 y		39 (35-43)		37 (34-40)		34 (30-39)	.28	.37	.11	.31

Outcomes after matched unrelated donor versus identical sibling hematopoietic cell transplantation in adults with AML: CIBMTR 2002-2006; Saber et al, Blood 2012

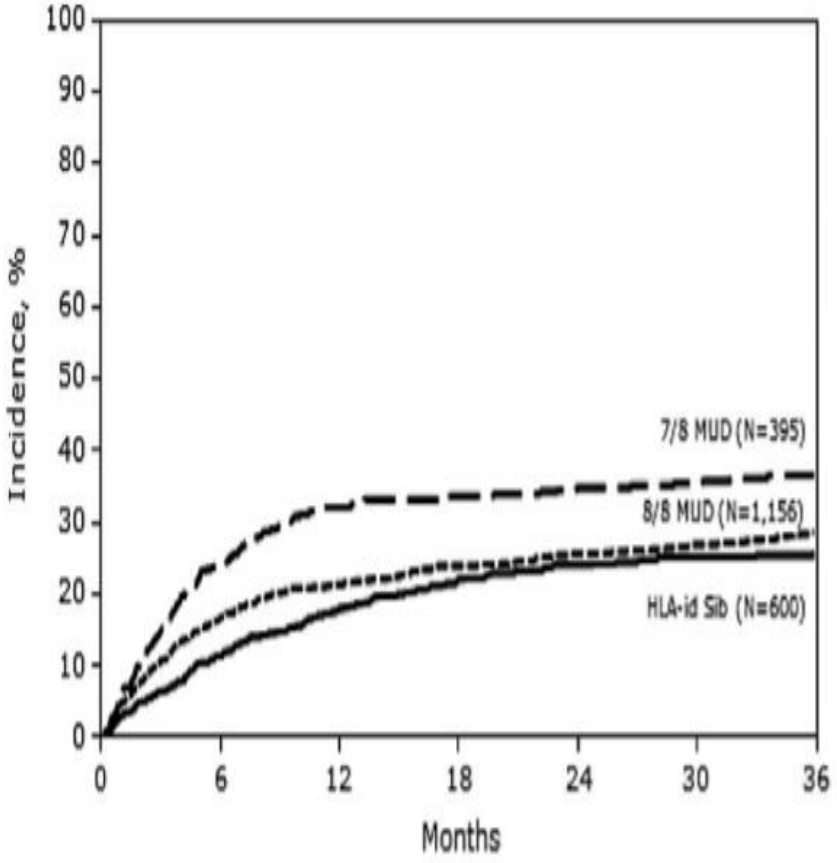


Figure 1. Adjusted probability of TRM in adult AML patients by donor type.

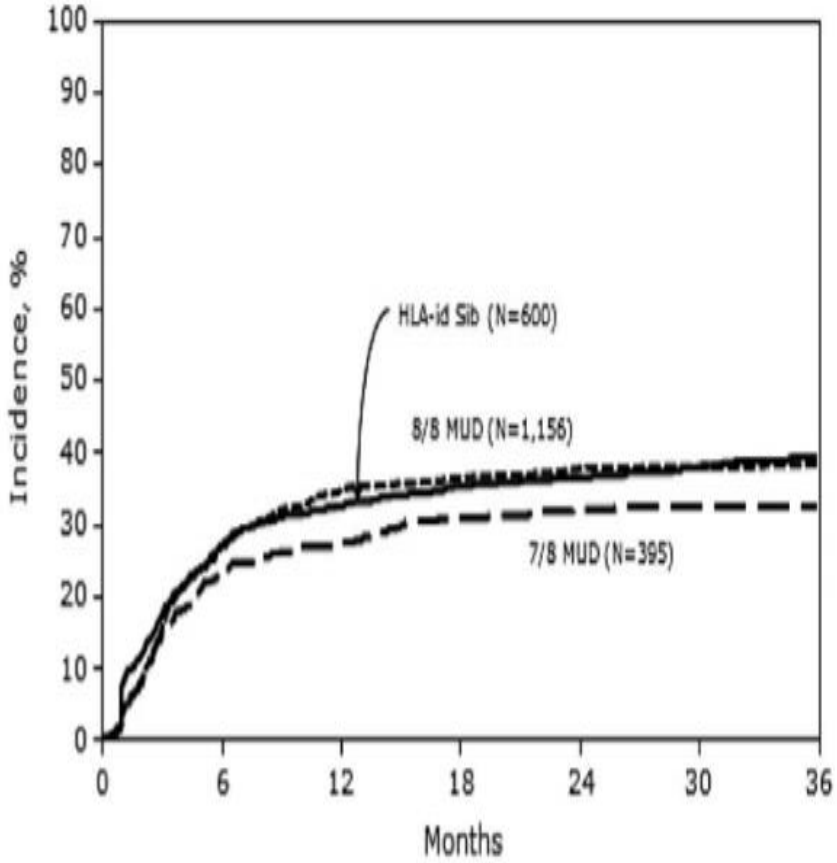


Figure 2. Adjusted probability of relapse in adult AML patients by donor type.

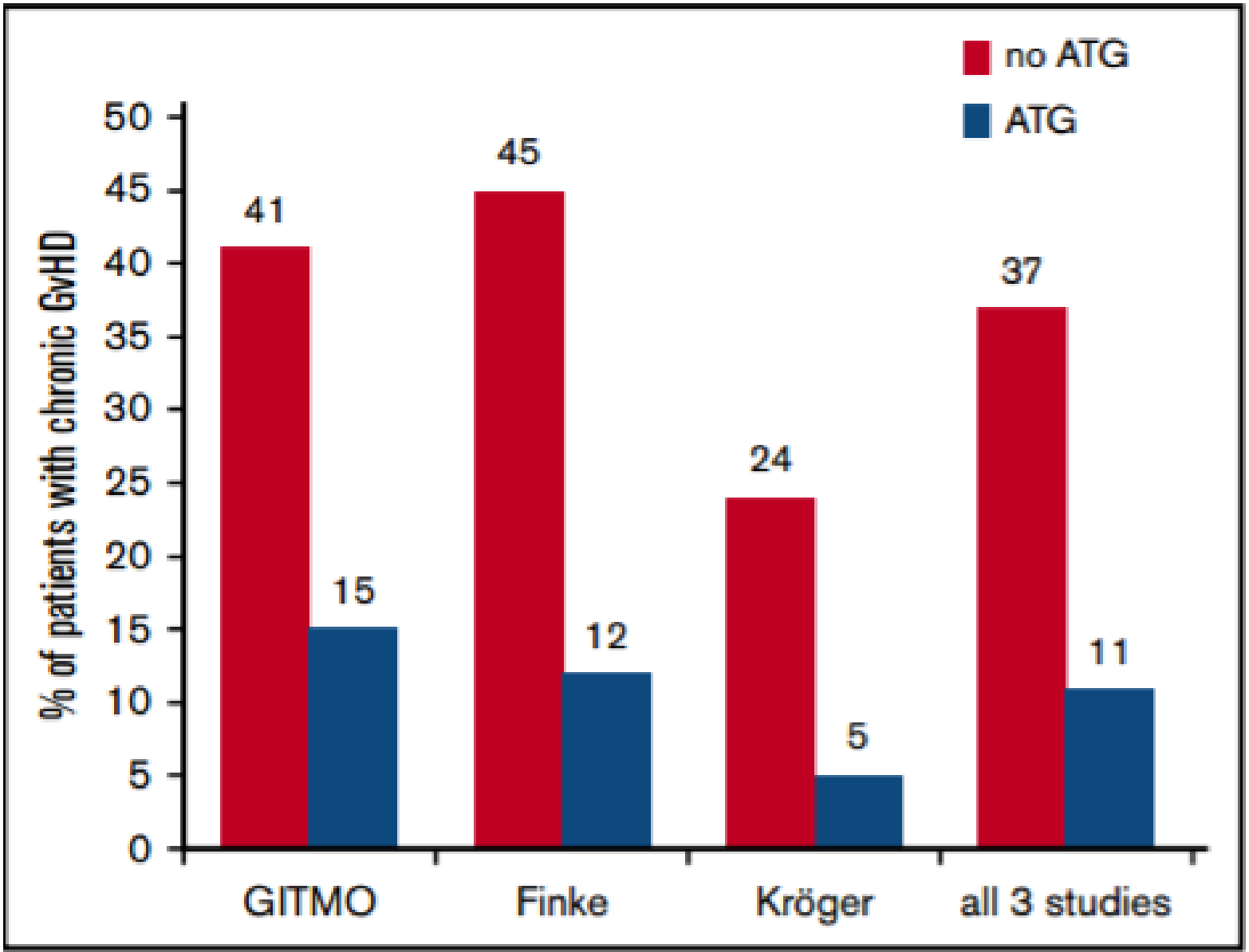
Causes of death in adult AML patients who underwent HLA-identical sibling (MRD) HCT or 8/8 or 7/8 MUD HCT

Cause, n (%)	MRD	8/8 MUD	7/8 MUD
Missing	6 (1.5)	7 (< 1)	3 (1)
Graft rejection	1 (< 1)	8 (1)	0
Infection	39 (10)	109 (14)	55 (20)
Interstitial pneumonitis	7 (2)	23 (3)	10 (4)
ARDS	4 (1)	20 (3)	2 (< 1)
GVHD	44 (11)	98 (13)	44 (16)
Primary disease	216 (54)	362 (47)	102 (37)
Organ failure	40 (10)	63 (8)	26 (9)
Secondary malignancy	5 (1)	5 (< 1)	1 (< 1
Hemorrhage	9 (2)	10 (1)	2 (< 1)
Accidental death	1 (< 1)	1 (< 1)	0
Vascular	2 (< 1)	4 (< 1)	3 (1)
Toxicity	0	25 (3)	5 (2)
Other cause	23 (6)	38 (5)	22 (8)
Total	397	773	275

ATG in allogeneic stem cell transplantation: standard of care in 2017? Point; Bacigalupo, Blood advances 2017

	GITMO[6,7]		Finke[8,9]		Kröger[10]		Total			
	ATG	noATG	ATG	noATG	ATG	noATG	ATG	noATG	RR	*P*
Patients, n	56	53	103	98	83	72	242	223	-	-
aGVHD II-IV, %	50%	70%	33%	51%	11%	18%	31%	46%	1.47	.001
aGVHD III-IV, %	23%	43%	11%	24%	2%	8%	12%	25%	2.08	.0003
cGVHD, %	37%	60%	26%	50%	22%	46%	28%	52%	1.83	.00001
ext cGVHD, %	15%	41%	12%	45%	5%	24%	11%	37%	3.43	.00001
NRM, %	39%	47%	19%	33%	14%	12%	24%	31%	1.27	.1
Relapse, %	23%	21%	33%	28%	32%	25%	29%	25%	0.84	.2
Survival, %	55%	56%	55%	43%	74%	77%	61%	59%	1.04	.6

ATG in allogeneic stem cell transplantation: standard of care in 2017? Point; Bacigalupo, Blood advances 2017



Post-transplant cyclophosphamide for GVHD prophylaxis in MUD/MMUD patients

Rationale for PTCy in MMUD/MUD

- In PBSC,

  - PTCy alone could reduce the risk of acute and chronic GVHD significantly.

  - ATG has been associated with decrease in chronic but not acute GVHD.

Post-transplant cyclophosphamide for GVHD prophylaxis in HLA matched sibling or matched unrelated donor SCT for patients with acute leukemia, on behalf of ALWP-EBMT

- PT-Cy alone (group 1): 78 pts
- PT-Cy plus 1 IS drug; CSA or MTX or MMF (group 2): 204 pts
- PT-Cy plus 2 IS drugs; CSA + MTX or CSA + MMF (group 3): 141 pts

- OS at 2 years : 50 (gr1), 52.2 (gr2) & 62.4% (gr3), p = 0.06.

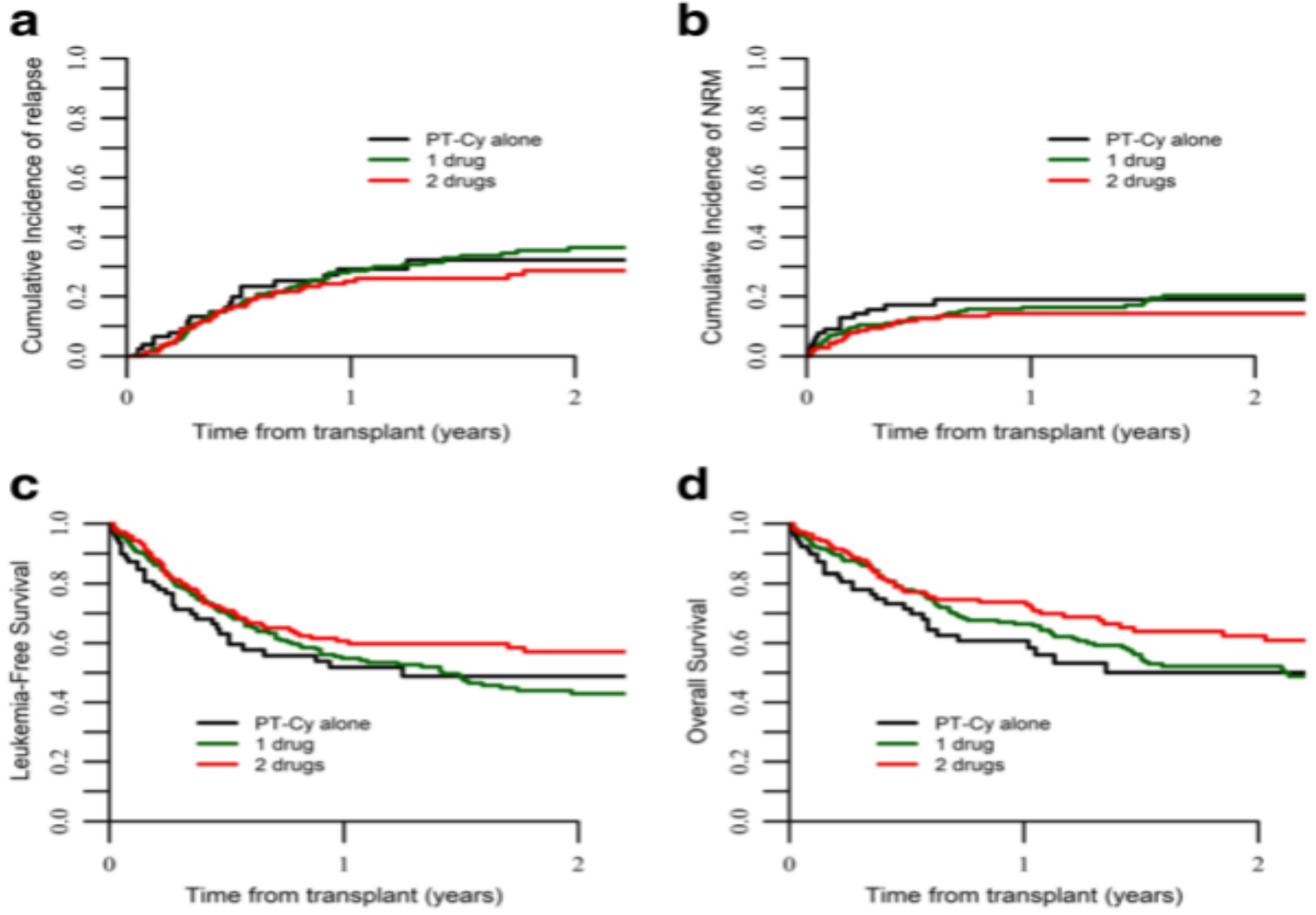
- In comparison to PT-Cy alone, the addition of 2 IS drugs was associated with reduced risk of extensive cGVHD (HR 0.25, p = 0.02).

- Use of BM and ATG were independently associated with reduced risk of extensive cGVHD.

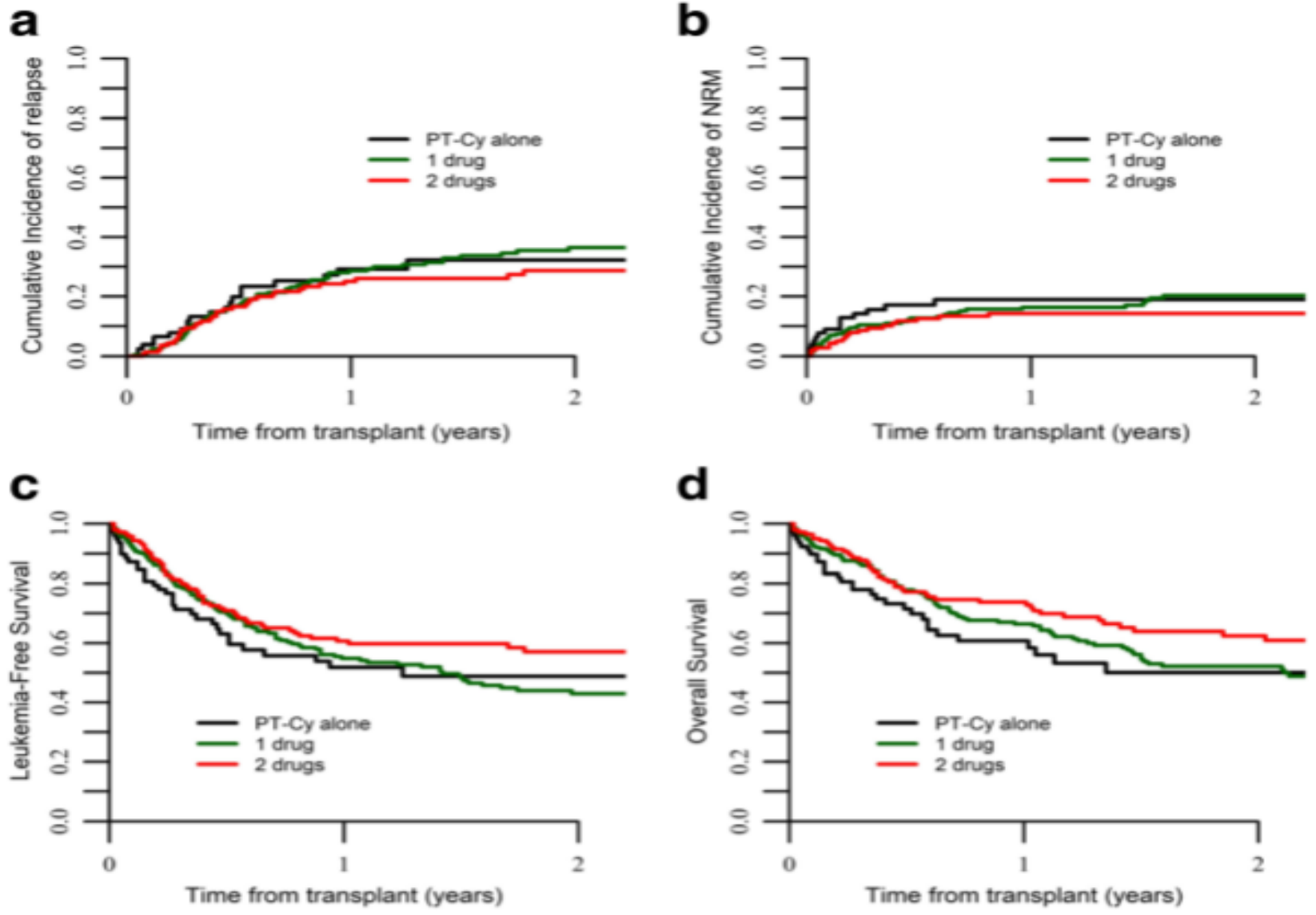
- Prognostic factors for NRM: addition of two IS drugs to PT-Cy (HR 0.35, p = 0.04), diagnosis of AML and disease status at transplant.

- Factors associated with increased OS: use of PT-Cy with two IS drugs (HR 0.49, p = 0.02), AML, and disease status at transplant.

Post-transplant cyclophosphamide for graft-versus-host disease prophylaxis in HLA matched sibling or matched unrelated donor transplant for patients with acute leukemia, on behalf of ALWP-EBMT



Post-transplant cyclophosphamide for graft-versus-host disease prophylaxis in HLA matched sibling or matched unrelated donor transplant for patients with acute leukemia, on behalf of ALWP-EBMT



Single Antigen–Mismatched Unrelated HSCT Using High-Dose Post-Transplantation Cyclophosphamide Is a Suitable Alternative for Patients Lacking HLA-Matched Donors

Jorge, Biol Blood Marrow Transplant 2018

- N= 86 recipients , PBSC: 92%
- MMUD (n = 26)
- MUD (n = 60)
- All PTCy MMUD were HLA 7/8: PTCy plus tacrolimus ± mofetil mycophenolate
- Acute GVHD grades II -IV at 100-day: MMUD 31% MUD: 22% , *P* = .59
- Moderate to severe chronic GVHD at 1 year: MMUD 22% MUD: 41% , *P* = 0.098

- NRM: MMUD 25% MUD: 18% , *P* = 0.52
- Relapse rate: MMUD 11% MUD: 19% , *P* = 0.18
- 2y PFS: MMUD 67% MUD: 54% , *P* = 0.68
- 2y OS: MMUD 72% MUD: 57% , *P* = 0.44

- Conclude: HLA 7/8 MMUD transplantation using PTCy plus tacrolimus is a suitable alternative for those patients who lack a MUD.

Post Transplant Cyclophosphamide (PTCy) with Anti-Thymocyte Globulin (ATG) Effectively Reduces the Severe (Grade III-IV) Acute Graft-Versus-Host Disease (GVHD) When Compared to ATG Alone in Matched Unrelated Donor (MUD) Allogeneic Hematopoietic Cell Transplants: Deotare, Blood 2016

Table 1: Comparison between ATG-CsA-MMf and ATG-PTCy-CsA cohorts when used as GVHD prophylaxis in MUD transplants

	ATG-CsA-MMF cohort	ATG-PTCy-CsA cohort
Total no of patients	27	28
Age (median, years)	54 (23-68)	58 (19-70)
Sex (M:F)	1.7:1	1.8:1
Disease Characteristics		
- AML	11	15
- ALL	5	3
- APL	0	1
- MDS	3	6
- CMML	1	1
- CML	1	1
- NHL	2	0
- CLL	2	0
- MF	1	1
- MDS/MPN-U	1	0
HLA matching		
- 10/10	20	22
- 9/10	7	6
Conditioning Regimen		
- FBT 400	17	11
- FBT 200	7	17
- Cy/TBI	2	0
- Bu/Cy	1	0
Acute GVHD	8	6
- Overall Gr I-II	1	5
- Overall Gr III-IV	7	1
- SR-GVHD	5	0
Chronic GVHD	13	NA
- Limited	8	
- Extensive	5	
Relapse of Primary Disease	1	3
Secondary Graft Failure	0	3
EBV reactivation	5	3
Survival	16	19

- PBSC

ATG-PTCy (+3/+4)-CsA:28 pts
- aGVHD: 26%
- Gr III-IV: 4%
-secondary graft failure: 10%
-EBV infection: 10%

ATG-CsA-MMF: 27 pts
- aGVHD: 22%
- Gr III-IV: 20% (p=0.085)

Treatment outcomes of MUD recipients in Ramathibodi Hospital; 2557-2561

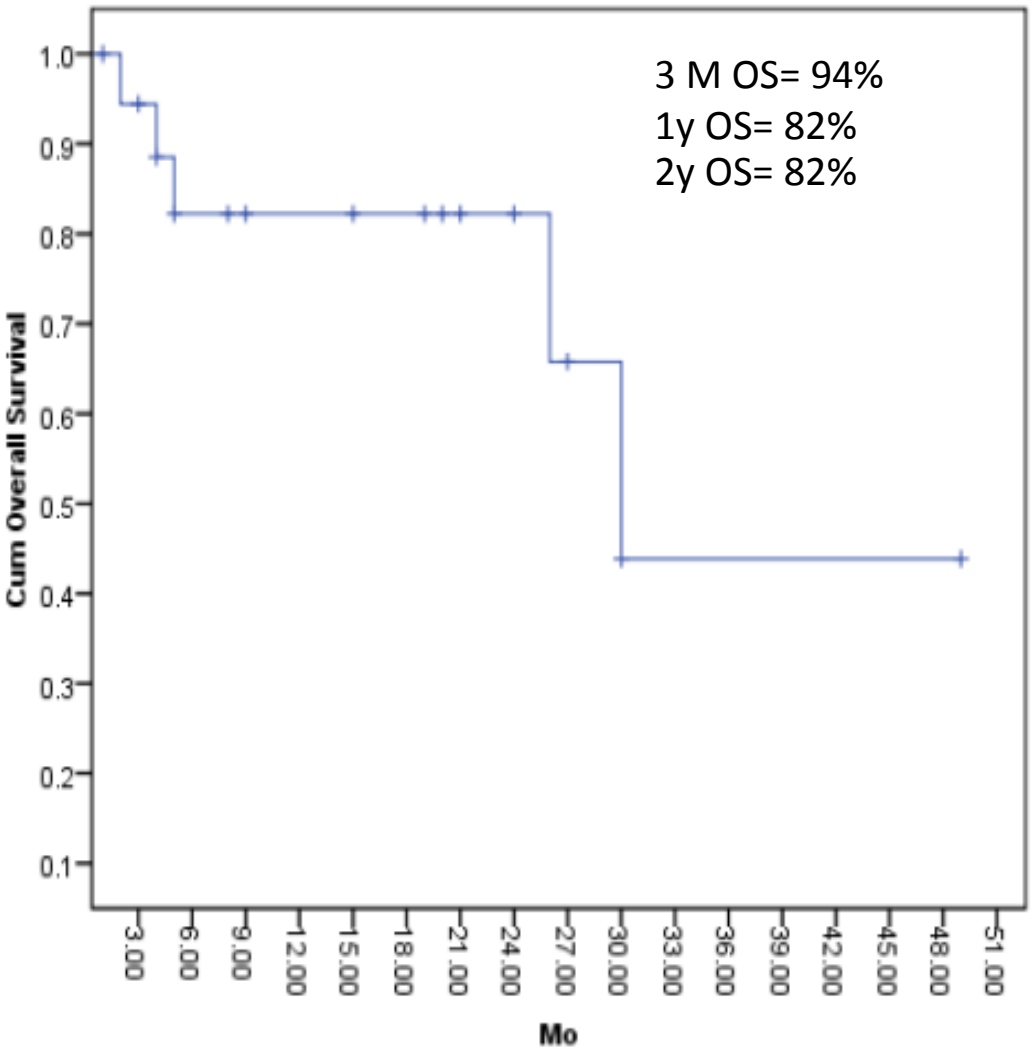
- Total: 20 pts, PBSC= 100%

- Median age: 38 y (17-60y), age> 50y= 6 pts

- ALL: 7 (Cy/TBI, Flu/Mel)
- AML: 8 (Flu/Bu, Flu/mel)
- MDS/PMF: 4 (Flu/Bu)
- BP-CML (T315I): 1 (Cy/TBI)

- GVHD prophylaxis: ATG/ CSA

- Full Match MUD: 11 pts (55%)
- MMUD: 9 pts (45%); HLA-A: 4 HLA-C: 1 HLA-DQ: 4



- Relapsed disease: 7 (35%)

- AML 4 (50%); t(8;21) (1) NPM+/ITD+ (1)
  APL (1) CN-AML (1)

- ALL: 2 (29%): Ph+ ALL (1) Ph-ALL (1)

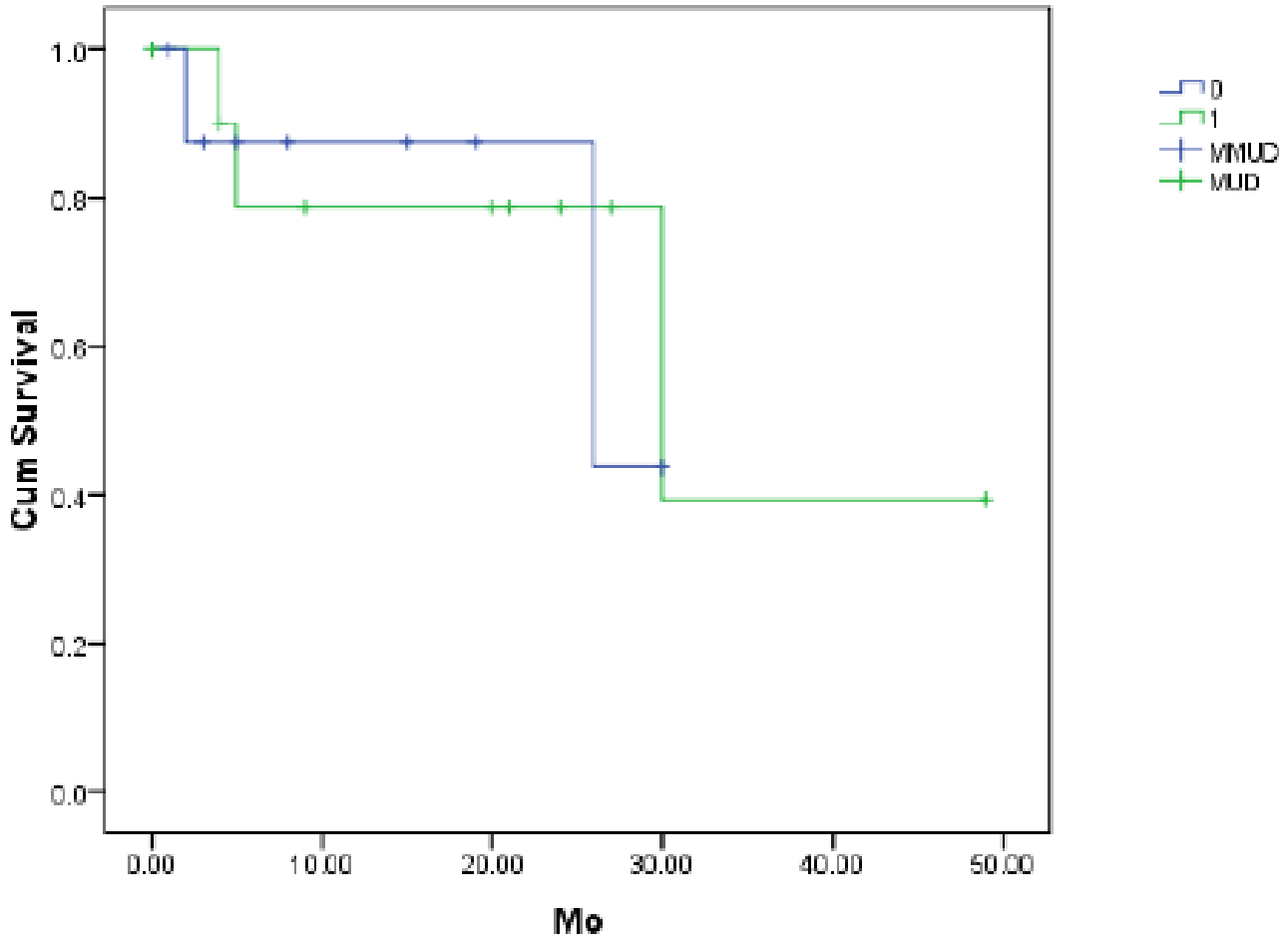
-BP-CML (T315I): 1

-GVHD: 6 (30%) grade 4= 1 pt

- EBV reactivation: 2

- PTLD: 1

- CMV reactivation: 10 (50%)


1.0
0.8
0.6
0.4
0.2
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Cum Survival
0.00
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Mo
0
1
MMUD
MUD

An overview of conditioning regimens for haploidentical stem cell transplantation with post-transplantation cyclophosphamide

Reference	Conditioning regimen	Diseases	HaploSCT (n)	Graft	aGVHD (II–IV)	NRM	Relapse rate	PFS or DFS
Myeloid malignancies								
Solomon et al. [32]	Flu/Bu/Cy regimen ($n = 5$) Fludarabine 30 mg/m^2 on days −7 to −2(total dose 180 mg/m^2) Busulfan 130 mg/m^2 on days −7 to −4 (total dose 520 mg/m^2) Cyclophosphamide 14.5 mg/kg on days −3 and −2 (total dose 29 mg/kg) Flu/Bu/Cy regimen ($n = 15$) (dose reduction due to mucositis) Fludarabine 25mg/m^2 on days −6 to −2(total dose 125 mg/m^2) Busulfan 110 mg/m^2 on days −7 to −4 (total dose 440 mg/m^2) Cyclophosphamide 14.5 mg/kg on days −3 and −2 (total dose 29 mg/kg)	Myeloid (30%-relapsed refractory) AML/CML (45%) Lymphoid (25%)	20	PB	30%	10% at 1yr	40% at 1yr	50% at 1yr (DFS)
Raiola et al. [33]	Thio/Bu/Flu regimen ($n = 35$; 8/35 received reduced dose busulfan) Thiotepa 5 mg/kg on days −6 and −5 (total 10 mg/kg) Busulfan 3.2 mg/kg IV on days −4 to −2 (total 9.6 mg/kg) Fludarabine 50 mg/m^2 on days −4 to −2 (total 150 mg/m^2) Flu/TBI regimen ($n = 15$) TBI 3.3 Gy on days −8 to −6 (total 9.9 Gy); Fludarabine 30 mg/m^2 on days −5 to −2 (total 120 mg/m^2)	AML 50% ALL 25% MPD 16%	50	BM (all)	12%	18% at 6 mo	22% at 18 mo	51% at 18 mo (DFS)
Bashey et al. [34]	Bu/Flu/Cy regimen ($n = 18$) Fludarabine 25 mg/m^2 on days −6 to −2 (total 125 mg/m^2) Busulfan 110–130 mg/m^2/day IV on days −7 to −4 Cyclophosphamide 14.5 mg/kg on days −3 and −2 (total 29 mg/m^2) Flu/Cy/TBI ($n = 35$) Fludarabine 30 mg/m^2 on days −6 to −2 Cyclophosphamide 14.5 mg/kg on days −6 and −5 (total 29 mg/m^2) Total body irradiation 2 Gy on day −1	AML 32% MDS/MPD 15% ALL 19%	53	PBSC ($n = 18$) BM ($n = 35$)	30%	7% at 2yr	33% at 2yrs	60% at 2yrs (DFS)
Pingali et al. [35]	Flu/Mel/Thio regimen Fludarabine 40 mg/m^2 on days −5 to −2 (total dose 160 mg/m^2) Mephalan 100–140 mg/m^2 on day −6 (total dose 100–140 mg/m^2) Thiotepa[a] 5 mg/kg on day −7 (total dose 5 mg/kg) (older patients/comorbidities received reduced doses of melphalan)	AML/MDS 66%	66	BM (94%)	25%	11.8% at 3yr	30.1% at 3yrs	56.5% at 3yrs[b] (PFS)
Solomon et al. [36][F]	Flu/TBI regimen Fludarabine 25 mg/m^2 on days −7 to −5 (total dose 75 mg/m^2) TBI 150 cGy BID on days −4 to −1 (total dose 12Gy)	AML 70% ALL 10% CML 15%	30	PB	44%	5% at 2yrs	19% at 2yrs	76% at 2yrs
Lymphoid malignancies								
Burroughs et al. [25]	Flu/Cy/TBI regimen Fludarabine 30 mg/m^2/d on days −6 to −2(total dose 150 mg/m^2) Cyclophosphamide 14.5 mg/kg/day on days −6 and −5 (total dose 29 mg/kg) 2 Gy TBI on day −1 (total dose 2 Gy)	HD 100%	28	BM	43%	9% at 2yrs	40% at 2yrs	51% at 2yrs (PFS)
Raiola et al. [37]	Flu/Cy/TBI regimen Fludarabine 30 mg/m^2/d IV daily on days −6 to −2 (total dose 150 mg/m^2) Cyclophosphamide 14.5 mg/kg IV on days −6 and −5 (total dose 29 mg/kg) 2 Gy TBI on day −1 (total dose 2 Gy)	HD 100%	26	BM (100%)	24%	4%	31% at 18 mo	63% at 3 yrs (DFS)
Castagna et al. [38]	Flu/Cy/TBI regimen Fludarabine 30 mg/m^2/d IV daily on days −6 to −2 (total dose 150 mg/m^2) Cyclophosphamide 14.5 mg/kg IV on days −6 and −5 (total dose 29 mg/kg) 2 Gy TBI on day −1 (total dose 2 Gy)	HD 55% NHL 39%	49	BM (80%)	26%	16% at 2yrs	19% at 2yrs	63% at 2yrs (PFS)
Kanakry et al. [34]	Flu/Cy/TBI regimen Fludarabine 30mg/m^2 for 5 days (total dose 150 mg/m^2) Cyclophosphamide 14.5 mg/kg for 2 days (total dose 29 mg/kg) 2 Gy TBI on one day (total dose 2 Gy) (only reduced intensity haploidentical included in table)	PTCL 100%	18	BM	16%	11% at 1 yr	34% at 1 yr	37% at 2 yrs (PFS)- includes all reduced intensity in study

Reference	Conditioning regimen	Diseases	(n)	Graft	aGVHD (II–IV)	NRM	Relapse rate	PFS or DFS
Kasamon et al. [39][F]	Flu/Cy/TBI regimen Fludarabine 30 mg/m^2 on days −6 to −2 (total dose 150 mg/m^2) Cyclophosphamide 14.5 mg/kg on days −6 and −5 (total dose 29 mg/kg) 2 Gy TBI on day −1 (total dose 2Gy)	NHL 75% HD 25%	151	BM	32%	16% at 1yr	31% at 1yr	40% at 3yrs (DFS)
Brammer et al. [40][F]	Flu/Mel/Thio of Flu/Mel/TBI regimen Fludarabine 40 mg/m^2 day on days −5 to −2 (total dose 160 mg/m^2) Mephalan 100–140 mg/m^2 on day −6 (total dose 100–140 mg/m^2) Thiotepa[a] 5 mg/kg on day −7 (total dose 5 mg/kg) or 2 Gy TBI Dose reduction to preferred regimen of Flu/Mel100 mg/m^2/TBI	HD 37% NHL 37% CLL/PLL 26%	19	BM	44%	11% at 2 yrs	26% at 2yrs	52% at 22 mo (PFS) (70% with FM100)

Conclusions

- Many studies suggest largely similar outcomes with peripheral blood haploidentical and MUD transplants for AML
- Slower count recovery after haploidentical allografts compared with those in MUD allografts
- PTCy plus 2IS drugs is an alternative therapy for MMUD

Acknowledge

Ramathibodi Comprehensive Cancer Center

Hematologists and nurses

Patients