Calling All Super Heroes

Cord Blood Unit Selection and Clinical Outcomes

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NATIONAL MARROW DONOR PROGRAM®

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Disclosures

The following faculty and planning committee staff have the following financial disclosures:

Name	Institution	Disclosure
Filippo Milano, MD, PhD	Fred Hutchinson Cancer Research Center	None
Kevin Tram	NMDP/Be The Match	None
Bernadette Anton	NMDP/Be The Match	None

Learning objectives

At the conclusion of this session, attendees will be able to:

- List advantages and disadvantages of cord blood transplantation
- Apply criteria for cord blood unit selection
- Compare outcomes after cord blood transplantation compared to other stem cell sources

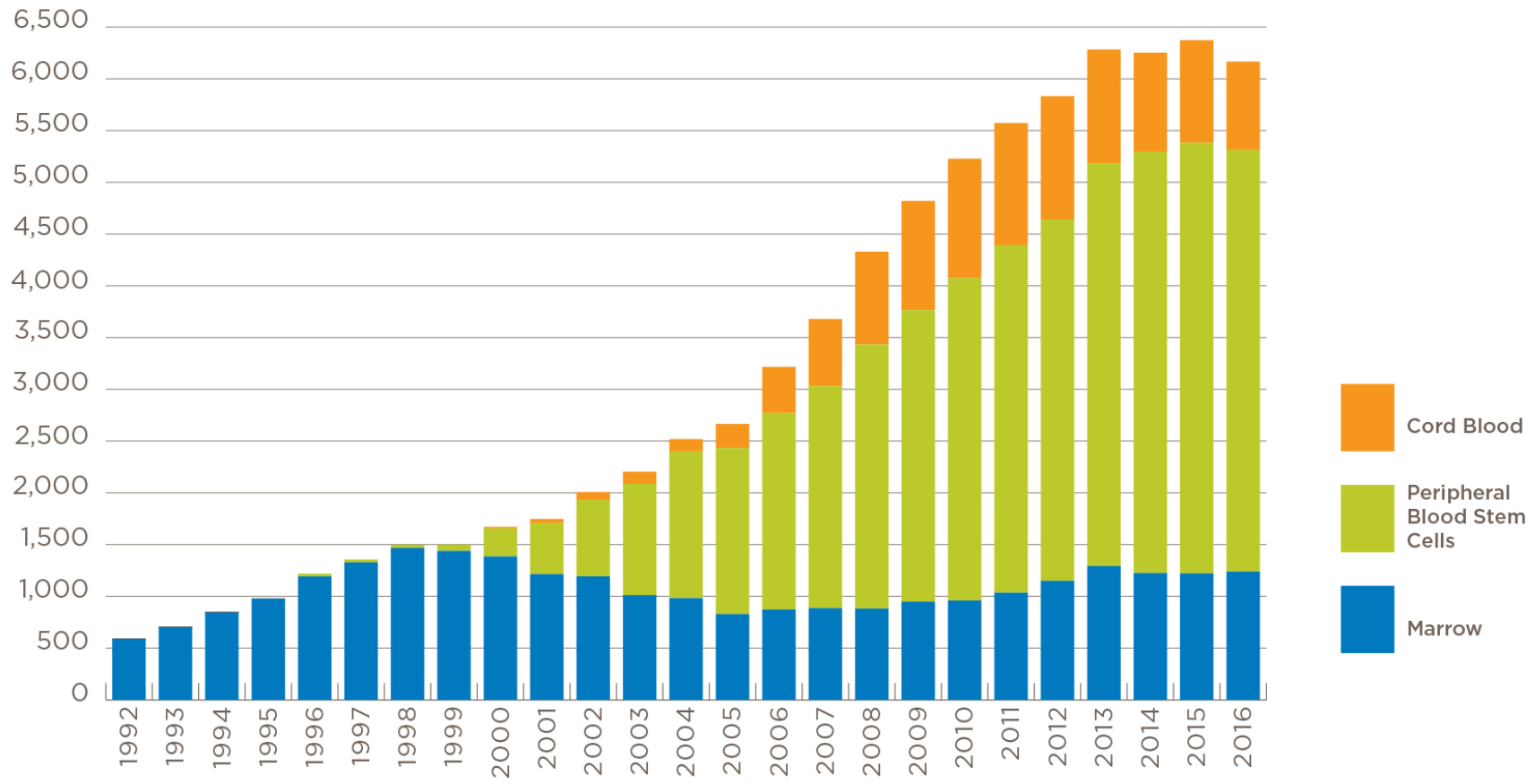
ADVANTAGES

1. Proof of principal
2. Easy to procure without risk
3. Decreased donor attrition and quick search time
3. Readily available, expands the donor pool , renewable
4. Better HLA tolerance
5. Suggestion of decreased cGVHD

DISADVANTAGES

1. LOW CELL DOSE
2. LOW CELL DOSE
3. LOW CELL DOSE
4. Delayed hematopoietic recovery
5. Increased graft failure, TRM and decreased OS
6. One time donation/No DLI
7. High cost upfront

Unrelated Transplants in USA



Source: National Marrow Donor Program/Be The Match FY 2016

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Current Hurdles in CBT

- COST of donor cell graft:

  dCBT $$$$

  URD $$

  Haplo $

- COST associated with CBT (1st 100 days)
  - Delayed engraftment
    - Neutrophils: TRM, infection, days in the hospital, supportive care (antimicrobials, GCSF)
    - Platelets: prolonged transfusion dependency, risk of DAH
  - Delayed immune reconstitution
  - More intensive supportive care (e.g., monitoring and preemptive therapy for viral reactivation) throughout first 100+ days
  - Lack of consistency among transplant centers

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  - **Lack of consistency among transplant centers**

Optimal Practices in Unrelated Donor CBT for Hematologic Malignancies

on behalf of the ASBMT CB SIG & the NMDP

DFCI/ Mass. General *(C. Cutler & K. Ballen-Adults)*
Duke *(J. Kurtzberg & M. Horwitz-Peds & Adults)*
Fred Hutch *(C. Delaney & F. Milano-Peds & Adults)*
MD Anderson *(A. Olson & E. Shpall-Adults)*
MSKCC *(J. Barker-Adults)*
U of MN *(C. Brunstein & J. Wagner-Peds & Adults)*
&
NMDP *(M. Boo, & S. Spellman)*

Optimal Practices: 6 Center Expert Opinion

- **Patient selection**- *disease, HCT-CI.*
- **Graft selection** - *search management, dose & match & quality unit, single vs double unit grafts, other (eg HLA antibodies).*
- **Conditioning**–*intensity, specific regimens*.
- **GVHD prophylaxis**- *CSA/ MMF vs other, ATG-yes/ no.*
- **Thaw & infusion**- *wash, thaw quality assessment, supportive care.*
- **Infection:** *prophylaxis, monitoring, & therapy*
- **Delayed engraftment & graft failure**
- **GVHD diagnosis & therapy**
- **Other complications** *(eg pre-engraftment syndrome, autoimmune hemolysis/ ITP).*

- **New technologies** - *expansion, homing, cellular therapy*.

Patient Selection: Diagnosis

Criteria	Boston	Duke	FHCRC	MDACC	MSKCC	U of MN
Standard remission requirement: AML/ MDS/ MPD	AML in morphol CR. (MPD avoided)	Peds: < 5% blasts Adults: AML < 5% blasts. MDS/ MPD < 10% blasts.	< 5% blasts by morphol/ flow cytometry.	AML in morphol CR.	≤ 10% blasts & not rapidly progressive disease.	Morphol CR.
Standard remission requirement: ALL/ aggressive NHL	ALL in morphol CR. NHL in CR or chemo-sensitive PR.	Peds: ALL in morphol CR. Adults: ALL <5%blasts. NHL in CR or chemo-sensitive PR.	ALL < 5% blasts by morphology & flow. NHL in CR or chemo-sensitive PR.	ALL in morphol CR. NHL in CR or chemo-sensitive PR.	ALL in morphol CR. NHL in CR.	ALL in morphol CR. NHL CR or chemo-sensitive PR.
Remission requirement other NHL/ HL	Chemo-sensitivity by CT or PET					

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Patient selection: Age & Organ function

Criteria	Boston	Duke	FHCRC	MDACC	MSKCC	U of MN
Age limit	Not defined	Not defined	< 70 years	≤ 65 years	< 70 years	≤ 75 years
Lower limit of acceptable organ function	EF ≥ 50%. Spirometry/ DLCOhb ≥ 50%. Bilirubin < 1.5 ULN. ALT/AST < 3 x ULN. Creat. clearance ≥ 50.	EF ≥ 50%. Spirometry/ DLCOhb ≥ 50%. Bilirubin < 1.5 ULN. ALT/AST < 3 x ULN. Creat. clearance ≥ 60	EF ≥ 45% if ablative (35% if NMA). Spirometry/ DLCOhb ≥ 50-70% (depending on intensity). Bilirubin ≤ 2 x ULN. ALT/AST < 3 x ULN. Creat. clearance ≥ 40-60.	EF ≥ 45%-50%. Spirometry/ DLCOhb ≥ 50% Bilirubin < 1.5 ULN. ALT/AST < 3 x ULN. Creat. clearance ≥ 60.		EF ≥ 35%. Spirometry/ DLCOhb ≥ 40%. Bilirubin < 2.0 x ULN. ALT/AST < 3 x ULN. Creat. clearance ≥ 40.

Mostly age limit around 70. Adequate organ function-slight variations in stringency & match conditioning intensity

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Conditioning Regimens

Criteria	Boston	Duke	FHCRC	MDACC	MSKCC	U of MN
High dose regimens	Cy 120/ Flu 75/ TBI 1200-1375	Peds* Cy 120/ Flu 75/ TBI 1320 Adults: TBI 1350/ Thio 10/ Flu 160	Cy 120/ Flu 75/ TBI 1320	Flu 100/ Clo 30/ Bu (4 days)/ TBI 200	Peds*: Cy 120/ Flu 75/ TBI 1320-1375. MSK: adults rarely get hi dose.	
Intermediate dose regimens	Flu 180/ Mel 100/ TBI 200	-	Treo 42/ Flu 150-200/ TBI 200	Flu 160/ Mel 140	Cy 50/ Flu 150/ Thio 10/ TBI 400. (Mel 100-140 Flu 150/ Thio 10 or Mel 140/ Flu 150).	-
NMA regimens	Cy 50/ Flu 150/ TBI 200		Cy 50/ Flu 150/ TBI 200-300	Cy 50/ Flu 150/ TBI 200		

Synergistic immunosuppression. Tailoring intensity to HCT-CI/ organ function. Move to intermediate intensity regimens

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GVHD Prophylaxis & G-CSF

Criteria	Boston	Duke	FHCRC	MDACC	MSKCC	U of MN
ATG inclusion	Yes	No		ATG including & excluding protocols	No	ATG including & excluding protocols
GVHD Prophylaxis	Tacro IV / sirolimus	Tacro IV / MMF IV	CSA IV / MMF IV	Tacro IV / MMF IV	CSA IV / MMF IV	CSA IV / MMF IV or MMF IV / sirolimus
Day of G-CSF start	Day +5	Peds: Day +1 Adults: Day +2	Day +1	Day 0	Day +7	Day +5

ATG-move away (ATG-PK).
GVHD prophylaxis-optimize CSA & MMF dosing.
New approaches-siro/ MMF?
GCSF-yes.

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CB Unit Selection

Criteria	Boston	Duke	FHCRC	MDACC	MSKCC	U of MN
Resolution of HLA-typing	8-allele HLA-A, -B, -C, -DRB1					
Donor-recipient HLA-match	≥ 4/6 alleles	Traditional ≥ 4/6 & ≥ 3/8 alleles	Traditional ≥ 4/6		Traditional ≥ 4/6 & ≥ 3/8 alleles	Traditional≥ 4/6 (& 8 allele)
Cell dose/kg: single unit	Singles not done	TNC ≥ 2.5				TNC ≥ 2.5 if ≥ 5-6/6 & ≥ 5.0 if 4/6. (CD34+ considered).
		CD34+ ≥ 1.5	CD34+ ≥ 2	CD34+ ≥ 1.0	CD34+ ≥ 1.5	
Cell dose/kg/unit: double unit	TNC ≥ 1.5/ unit	TNC ≥ 1.5/ unit				
		CD34+ ≥ 1.0/ unit	CD34+ ≥ 2.0/ unit	CD34+ ≥ 1.0	CD34+ ≥ 1.0/ unit	CD34+ considered.

CB Unit Selection

Criteria	Boston	Duke	FHCRC	MDACC	MSKCC	U of MN
Avoidance of units against which recipient has DSA	Yes	Not if Malig.	Yes		Usually not if Malig.	Yes
Bank of origin major criteria in selection	Yes					
Netcord-FACT accreditation considered	No	Yes				
Use of RBC replete units	Sometimes	No				
Testing attached segment for identity	Yes					
Viability testing at thaw (day 0)	Yes: % viable CD34+ cells by flow (7AAD)					
Back-up unit policy	Haplo-donor if possible	1-2 domestic units	No		1-2 domestic units	Haplo-donor if possible

Thaw & Infusion: RBC-depleted

Criteria	Boston	Duke	FHCRC	MDACC	MSKCC	U of MN
Manual/ automated wash or dilution	Manual wash	Automated wash	Dilution if recipient > 20 kg. Otherwise manual wash.	Automated wash	Dilution if recipient > 20 kg. Otherwise manual wash.	Manual wash
Final volume	As appropriate	Peds: < 5 mls/kg Adults: 50 mls	8-fold dilution	~ 50 mls	8-fold dilution	~ 100 mls
Pre-medication	Diphenhydramine					
	Hydrocort	Tylenol Hydrocort	Tylenol Hydrocort	Hydrocort	Tylenol Lorazepam Hydrocort	Tylenol
Hydration	500 mls pre-infusion	Peds: Twice maintenance for 4-6 hours. Adults: maintenance fluids.	Twice maintenance 4-6 hours pre- & 24 hours post-CBT	Twice maintenance 2 hours pre- & 4 post-CBT	Twice maintenance 4-6 hours pre & 12 hours post. Maintain fluid balance.	4-6 hours pre- & 12-24 hours post
Minimum infusion time	~ 45 minutes/ unit	Peds: ~ 15 minutes Adults: ~ 45 minutes	~ 30 minutes/ unit		~ 30-45 minutes/ unit	By gravity for small children. Otherwise ~ 45 minutes/ unit
Rx of hypertension	Individualized to patient	IV hydrallazine	IV hydralazine + furosemide	Anti-hypertensive +/- furosemide	IV hydrallazine ± furosemide	As indicated

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Wash or dilution. Pre-meds & supportive care critical.

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Optimal Practices: Aim

• In experienced centers, CBT survival is comparable to the gold standard of HLA-matched URD transplants.

• Centers have developed expertise in CBT that is critical to optimize outcomes.

• Sharing this expertise will improve outcomes & reduce cost.

• CB SIG forum will facilitate information exchange, sharing of ideas & stimulate research into areas of controversy that will further improve CBT.

Current State

Conventional Donor Transplant (BM/PBSC)

Unrelated Donor Transplant Cord Blood

- **Lower** risk of early TRM
- **Higher** risk of relapse

- **Higher** risk of early TRM
- **Lower** risk of relapse

Overall Survival = Overall survival

High-risk disease

Conventional Donor Transplant (BM/PBSC)

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Unrelated Donor Transplant Cord Blood

- **Higher** risk of early TRM
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Overall Survival = Overall survival

Study Design

- Between January 2006 and December 2014 we retrospectively analyzed outcomes for 582 patients undergoing first allogeneic hematopoietic stem cell transplantation for hematologic malignancies with either umbilical cord blood (CBT) or unrelated donor (URD).
- In the CBT group (n=140) selected cord blood units were required to be matched to the recipient at ≥ 4 of the 6 HLA loci based on intermediate resolution typing at HLA-A and –B and allele-level for HLA-DRB1.
- All patients received a double CB graft except for 16 patients (11%) who received a single CB graft. In addition, 39 (28%) patients received an ex vivo expanded CB unit as part of either a single or double CBT.
- In the URD group (n=442), patients received either HLA 10/10 (n=334) allele matched URD (MURD) or 9/10 (n=98) allele mismatched URD (MMURD).

N Engl J Med. 2016 Sep 8;375(10):944-53

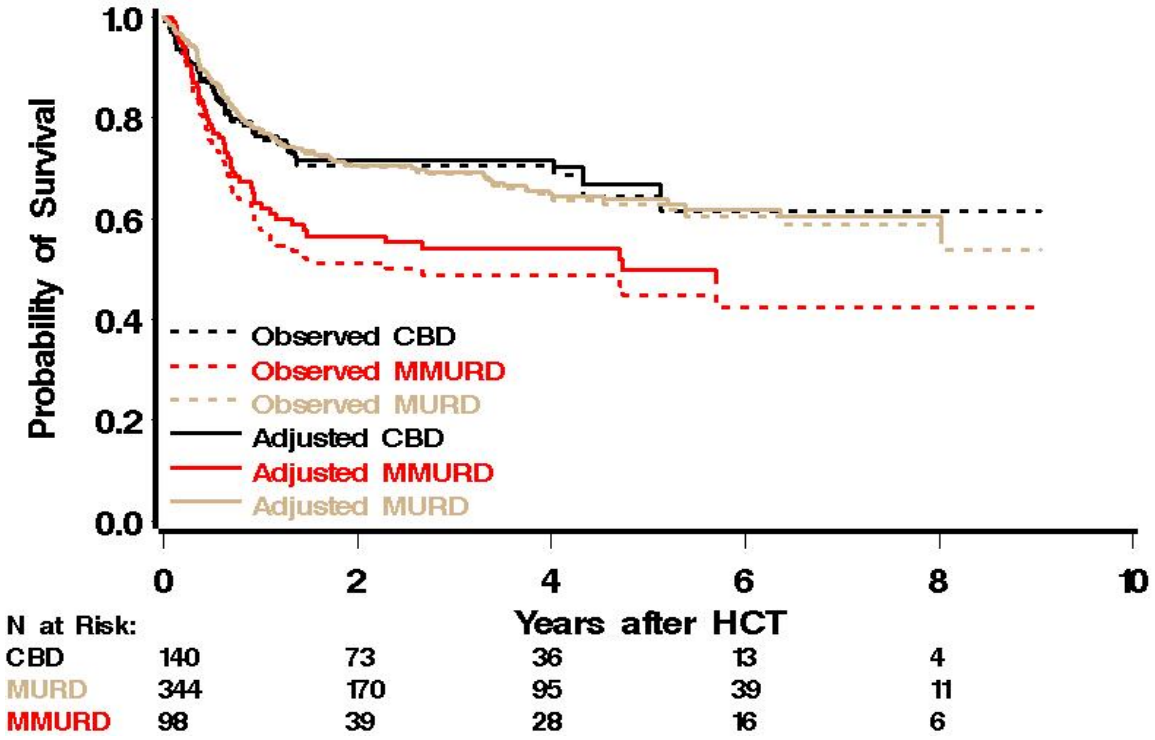
Patient characteristics (1)

	CBT (n=140)	MURD (n=344)	MMURD (n=98)
Age in years, (range)	29 (0.6-64)	40 (1-67)	45 (2-64)
Gender, Female, n (%)	68 (48)	150 (43)	45 (46)
Weight in kg, (range)	70 (9-112)	76 (13-173)	77 (12-142)
Race, n (%)			
Caucasian	64 (45)	296 (85)	76 (77)
Other	76 (55)	50 (15)	22 (23)
CMV serostatus, n (%)			
Pos	86 (62)	179 (52)	47 (48)
Neg	54 (38)	167 (48)	51 (52)
Diagnosis, n (%)			
AML	73 (52)	177 (51)	52 (53)
ALL	51 (36)	106 (31)	28 (29)
MDS	16 (12)	63 (18)	18 (18)
Presence of minimal residual disease — no./total no. (%)	**45/137 (33)**	**104/331 (31)**	**35/90 (39)**

Patient characteristics (2)

	CBT (n=140)	MURD (n=344)	MMURD (n=98)
Stem cell source, n (%)			
CB	140 (100)	-	-
BM	-	107 (31)	29 (30)
PB	-	237 (69)	69 (70)
Disease risk, n (%)			
Low/Intermediate	93 (66)	276 (80)	77 (79)
High or Very High	47 (34)	68 (20)	21(21)
Conditioning regimen, n (%)			
FLU/CY/TBI 1320 cGy	97 (69)	-	-
TREO/FLU/TBI 200 cGy	43 (31)	64 (19)	7 (7)
BU with either Cy or Flu	-	129 (37)	54 (55)
CY/TBI 1200 or 1320 cGy	-	153 (44)	37 (38)
GVHD Prophylaxis, n(%)			
CSA+MMF	140 (100)	-	-
FK506+MTX	-	268 (77)	98 (100)
FK506+MMF+CY	-	76 (23)	-
Other			

Overall Survival



Survival at 4 years

CBT	71%
MURD	63%
MMURD	49%

	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Cord Blood	1		1	
MURD	1.04 (0.73-1.47)	0.85	1.10 (0.76-1.60)	0.61
MMURD	1.84 (1.23-2.74)	**0.003**	1.89 (1.22-2.93)	**0.004**

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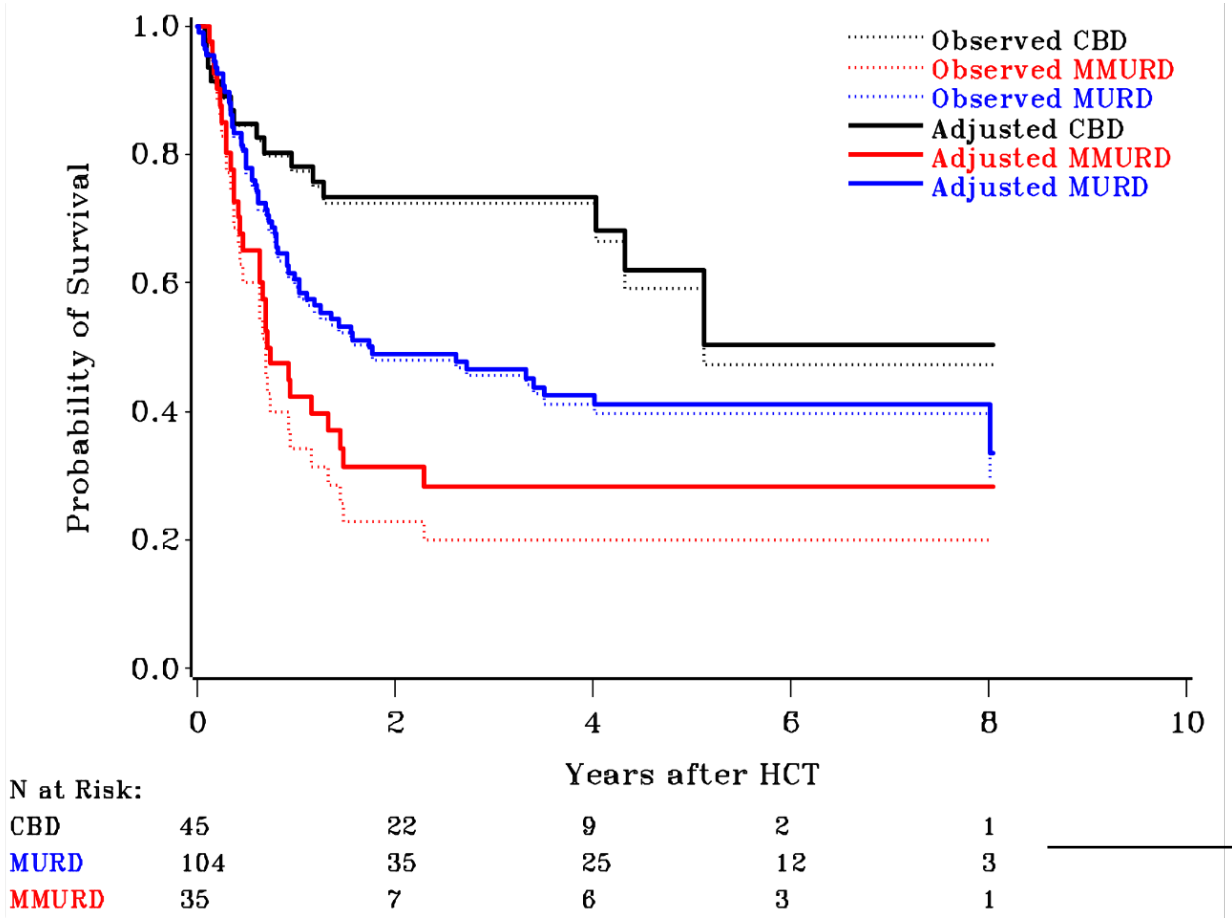
Risk of mortality in patients with minimal residual disease



Survival at 4 years

CBT	67%
MURD	40%
MMURD	20%

	Adjusted HR (95% CI)	p-value
Cord Blood	1	
MURD	1.69 (0.94–3.02)	0.08
MMURD	2.92 (1.52–5.63)	**0.001**

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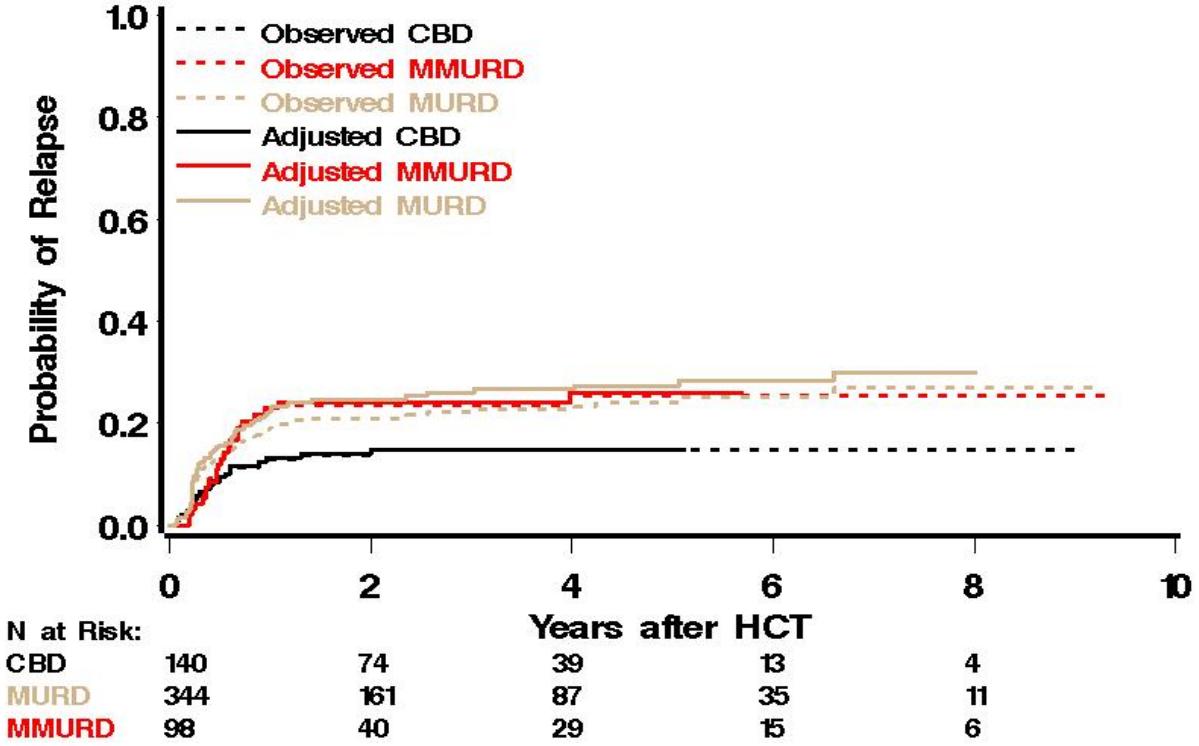
Unadjusted and adjusted estimates of probability of relapse

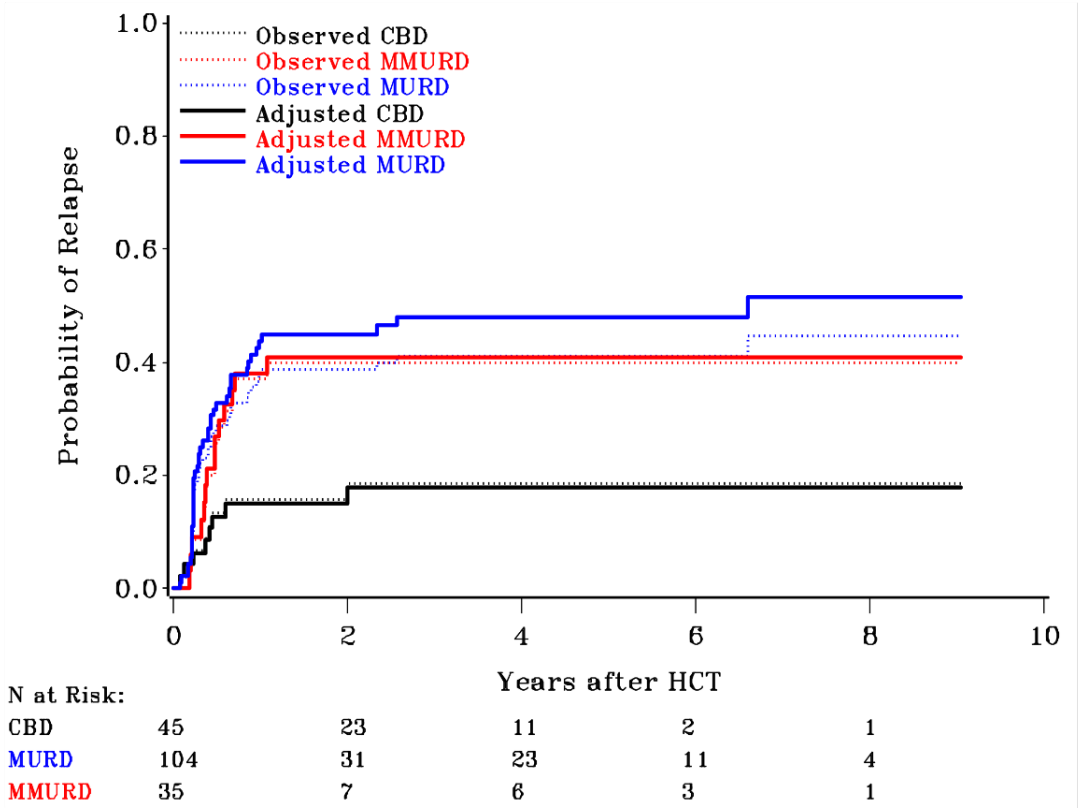


Relapse at 4 years

CBT	15%
MURD	24%
MMURD	25%

	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Cord Blood	1		1	
MURD	1.60 (0.98-2.61)	**0.06**	1.95 (1.16-3.27)	**0.01**
MMURD	1.90 (1.05-3.43)	**0.03**	1.97 (1.04-3.72)	**0.04**

Risk of relapse in patients with minimal residual disease



Relapse at 4 years

CBT	19%
MURD	44%
MMURD	40%

	Adjusted HR (95% CI)	p-value
Cord Blood	1	
MURD	2.92 (1.34–6.35)	**0.007**
MMURD	3.01 (1.22–7.38)	**0.02**

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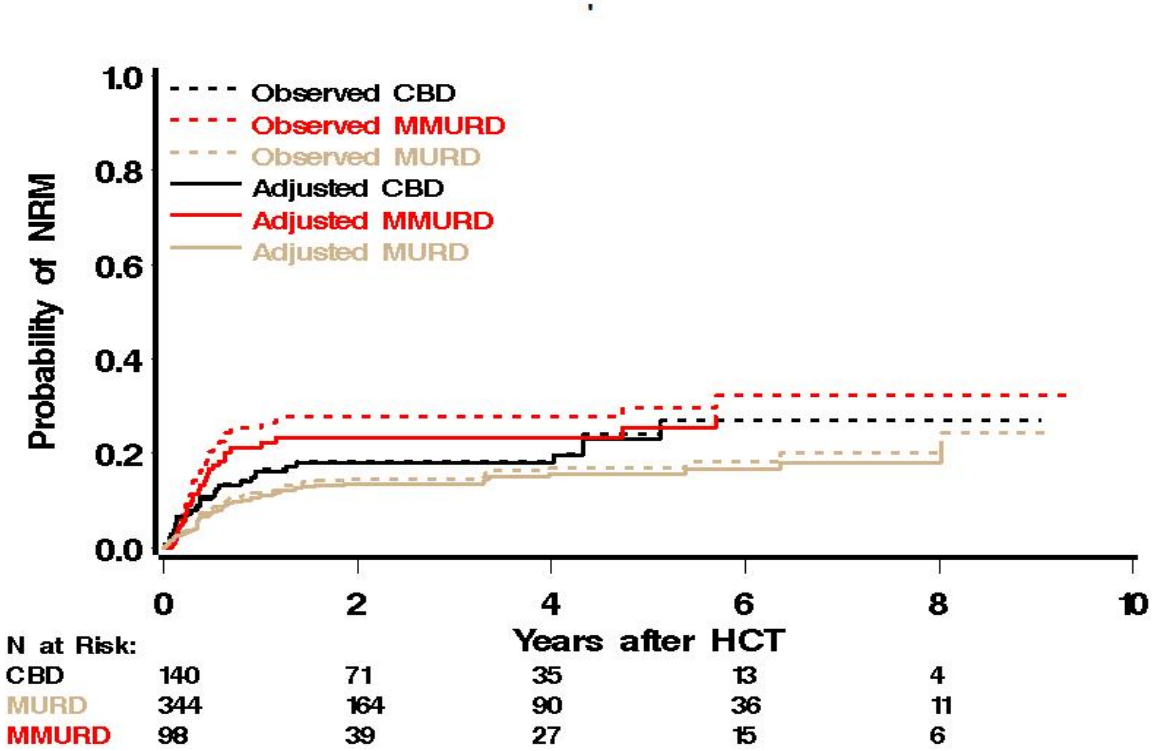
Impact of Minimal Residual Disease on mortality and relapse

Each cohort of patients had approximately 30% of patients with evidence of MRD

Donor Group	Overall Mortality		Relapse	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
MURD	2.34 (1.59–3.45)	<0.001	3.23 (2.01–5.19)	<0.001
MMURD	2.33 (1.32–4.09)	0.003	3.37 (1.39–8.15)	0.007
CBT	1.09 (0.57–2.08)	**0.80**	1.43 (0.58–3.57)	**0.44**

In contrast to MURD and MMURD HCT, pre-transplant MRD is <u>not</u> associated with increased risk of relapse or mortality after myeloablative CBT.

Unadjusted and adjusted estimates of probability of non-relapse mortality



NRM at 4 years

CBT	18%
MURD	17%
MMURD	28%

	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Cord Blood	1		1	
MURD	0.78 (0.50-1.22)	0.29	0.72 (0.44-1.18)	0.19
MMURD	1.53 (0.91-2.56)	0.11	1.44 (0.81-2.55)	0.21

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Chronic GVHD

Conventional Donor Transplant (BM/PBSC)

Unrelated Donor Transplant Cord Blood

- **Lower** risk of early TRM
- **Higher** risk of relapse

- **Higher** risk of early TRM
- **Lower** risk of relapse

Overall Survival = Overall survival

Chronic GVHD Severity and Function Status after Alternative Donor Hematopoietic Cell Transplantation

Giancarlo Fatobene, Filippo Milano and Mary E.D. Flowers

ASH Meeting 2017

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Comparison of Chronic GVHD Severity and Functional Status after Alternative Donor HCT

- Retrospective study
- All patients > 18 y/o
- First alternative donor hematopoietic cell transplant for any diagnosis in Seattle between 2006 to 2015

Alternative hematopoietic cell donors included:

- 1 allele mismatched unrelated adult mobilized blood
- Cord blood unrelated (single or double)
- Haploidentical related bone marrow or mobilized peripheral blood

Alternative Donor Groups Included

- 1-allele mismatched at an HLA-A, B, C or DR locus at any HLA-typing resolution unrelated adult **(1-mMUD)**
- 4-6/6-HLA-matched umbilical cord blood **(UCB)**
- Related HLA-haploindentical **(R-HAPLO)**

Patient characteristics (n=396)

Characteristic	Alternative donor group		
	Unrelated mismatched (N = 145)	Cord blood (N = 163)	Related haploidentical (N = 88)
Age at transplant (years),Median (range)	55 (22-77)	42 (18-73)	48 (18-75)
Female – no. (%)	54 (37)	83 (51)	35 (40)
Diagnosis – no. (%)			
AML	53 (37)	82 (50)	21 (24)
MDS	31 (28)	23 (14)	6 (7)
ALL	17 (12)	37 (23)	5 (6)
CLL	9 (6)	2 (1)	3 (3)
CML	11 (8)	7 (4)	2 (2)
HL	1 (1)	.	25 (28)
NHL[1]	12 (8)	7 (4)	21 (24)
MM[2]	8 (6)	.	4 (5)
Non-malignant/other[3]	3 (2)	5 (3)	1 (1)

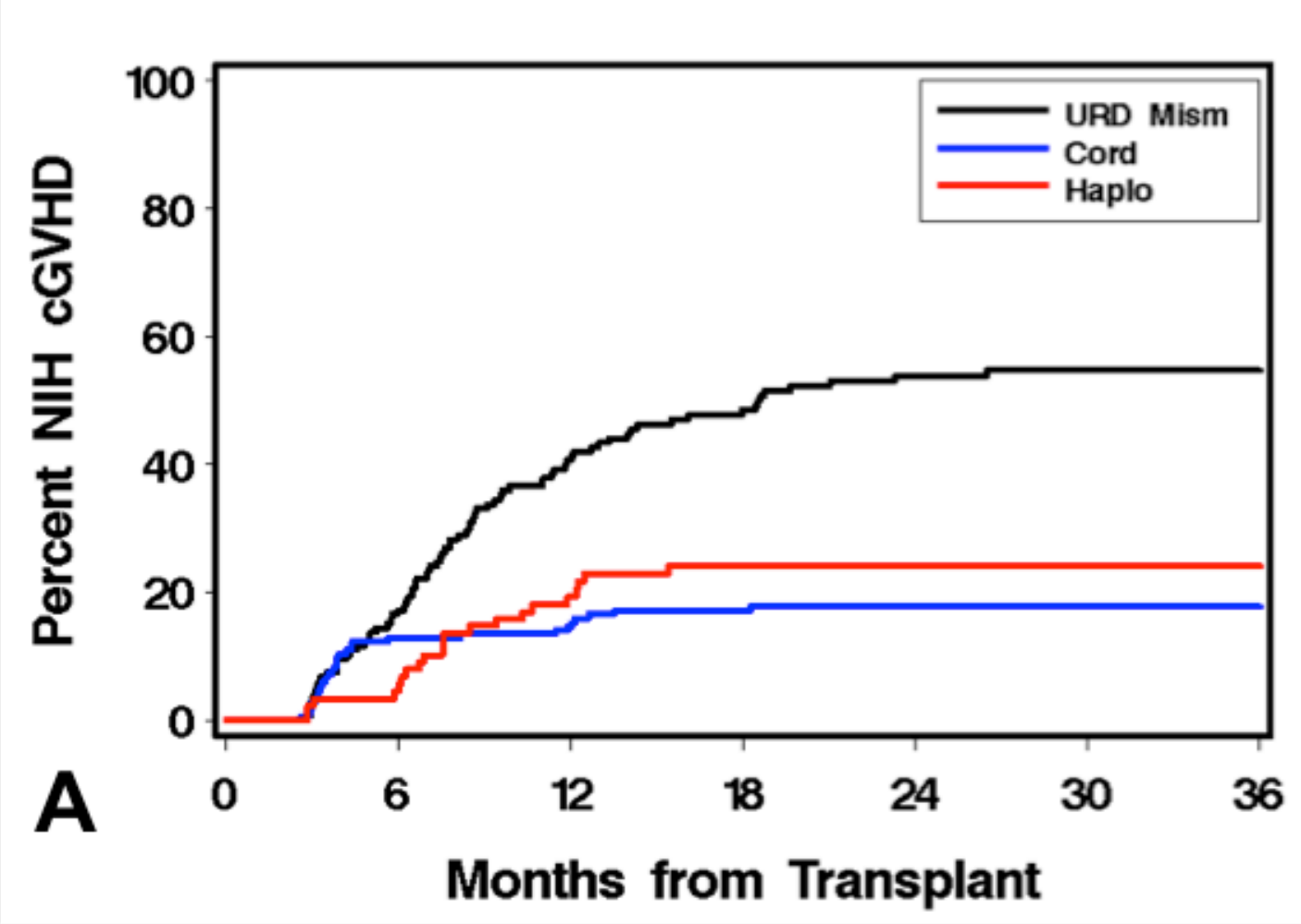
Patient characteristics (2)

Population Characteristic	Alternative donor group		
	Unrelated mismatched (N = 145)	Cord blood (N = 163)	Related haploidentical (N = 88)
Conditioning regimen – no. (%)			
NMA/RIC	69 (48)	43 (26)	71 (81)
MA	76 (52)	120 (74)	17 (19)
GVHD prophylaxis – no. (%)			
CNI and MMF	71 (49)	163 (100)	.
CNI and MTX	71 (49)	.	.
CY and CNI and MMF	.	.	87 (99)
Other	3 (2)	.	1 (1)
HLA-match – no. (%)			
7/8	145 (100)	.	1 (1)
4-6/8	.	.	6 (7)
5-6/6	.	35 (21)	.
4/6	.	128 (79)	1(1)
3/6	.		80 (91)
Follow-up post-HCT (months), Median, (range)	46 (4-131)	48 (4-121)	60 (<1-123)

Number of patients with chronic GVHD

- Of 396 alternative donor HCT recipients transplanted between 2006 and 2015, **129** developed chronic GVHD and were included in this study.

Cumulative incidence at 3 years



Chronic GVHD (3-year CI) developed after HCT in 129 patients

79 of 145 1-mMUD recipients (55%)

29 of 163 UCB recipients (18%)

21 of 88 R-HAPLO recipients (24%)

Chronic GVHD Characteristics (n=129)

	Unrelated Mismatched (N =79)	Cord blood (N = 29)	P[1]	Related Haploidentical (N = 21)	P[2]
NIH severity at diagnosis – no. (%)					
Mild	13 (16)	11 (38)		5 (24)	
Moderate	46 (58)	17 (59)	0.008	11 (52)	0.74
Severe	20 (25)	1 (3)		5 (24)	
Type of onset – no. (%)					
De novo	21 (27)	4 (14)		0	
Quiescent	7 (9)	1 (3)	0.19	5 (24)	0.01
Progressive	51 (65)	24 (83)		16 (76)	

[1] Cord blood vs. mismatched unrelated

[2] Haploidentical vs mismatched unrelated

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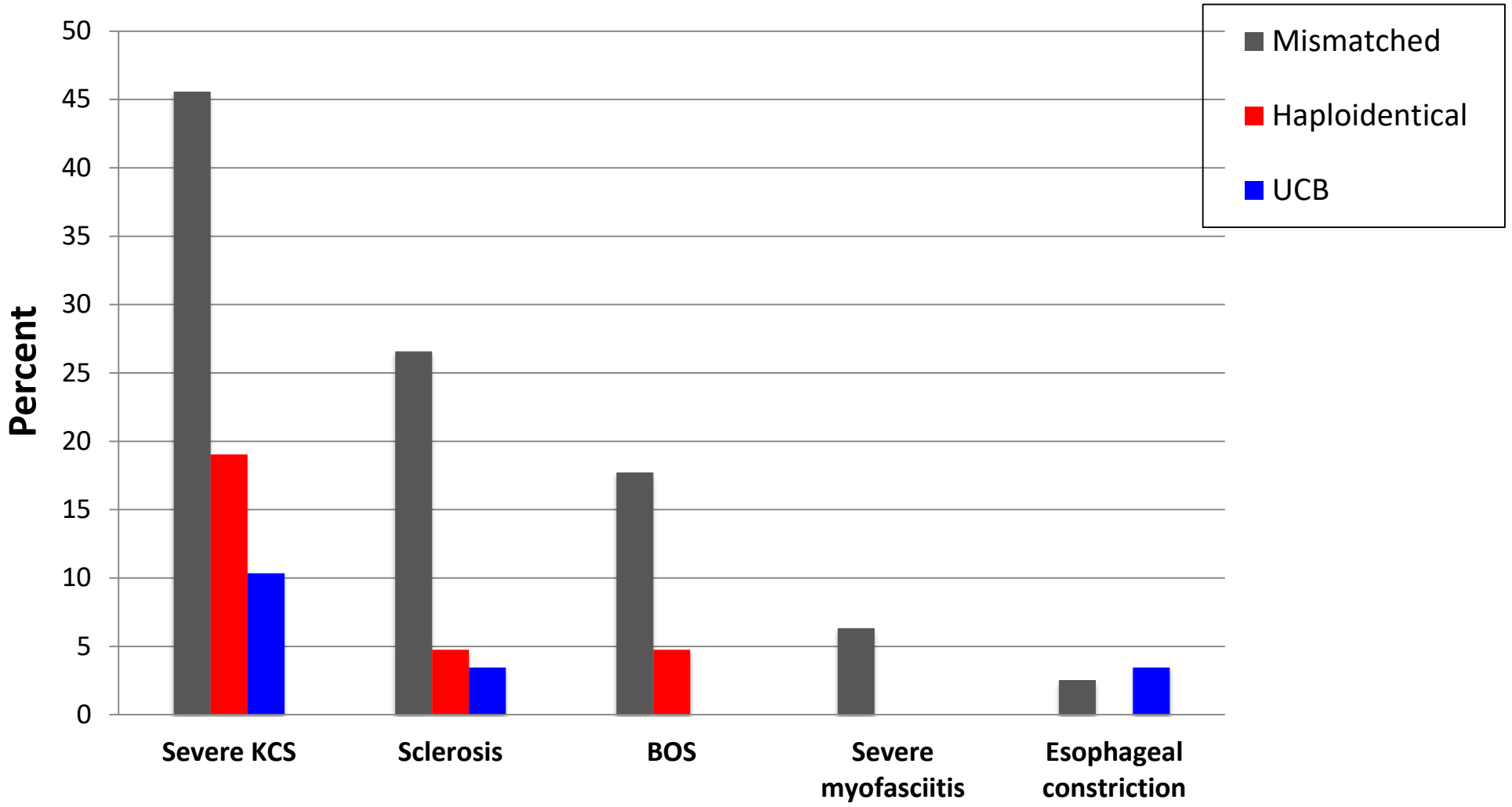
Chronic GVHD Characteristics (n=129)

	Unrelated Mismatched (N =79)	Cord blood (N = 29)	P[1]	Related Haploidentical (N = 21)	P[2]
Sites involved at onset – no. (%)					
Skin	59 (75)	16 (55)	0.05	16 (76)	0.89
Eyes	30 (38)	5 (17)	**0.04**	5 (24)	0.23
Mouth	74 (94)	26 (90)	0.48	16 (76)	**0.02**
Liver	27 (34)	3 (10)	**0.01**	2 (10)	**0.03**
Lung	2 (3)	2 (7)	0.29	1 (5)	0.59
Gastrointestinal tract	28 (35)	20 (69)	**0.002**	6 (29)	0.55
Joint	5 (6)	0	0.17	0	0.24
Genital	8 (10)	1 (3)	0.27	1 (5)	0.45
Eosinophilia at onset – no (%)	19 (24)	1 (3)	**0.01**	3 (14)	0.34

Distribution of chronic GVHD Manifestations associated with severe morbidity



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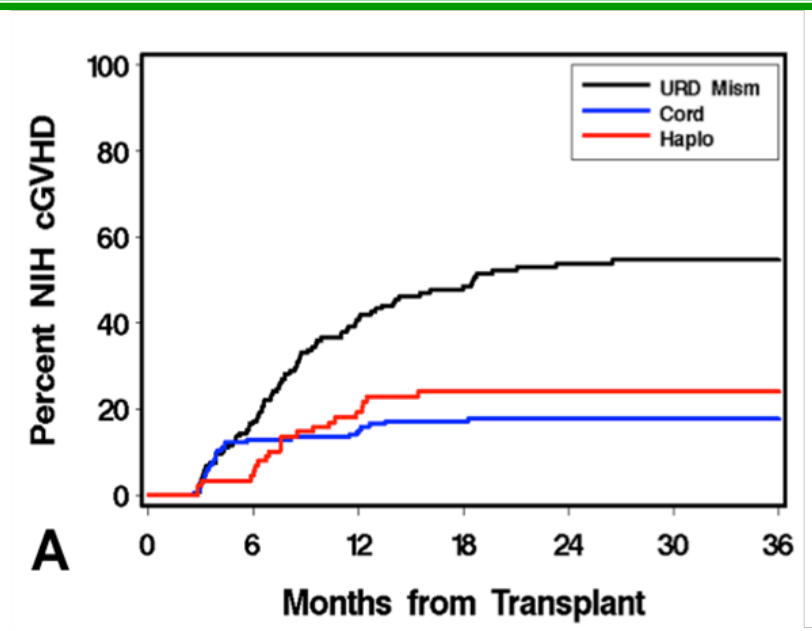

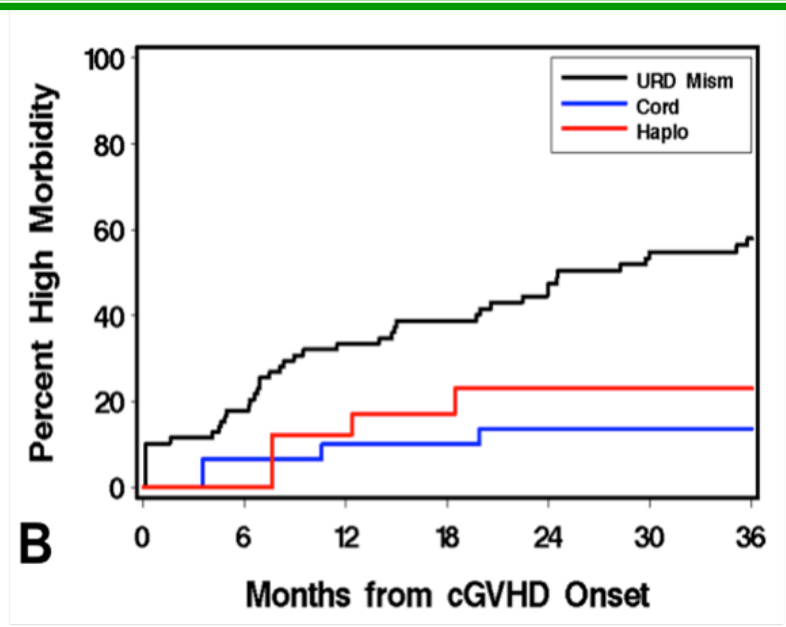

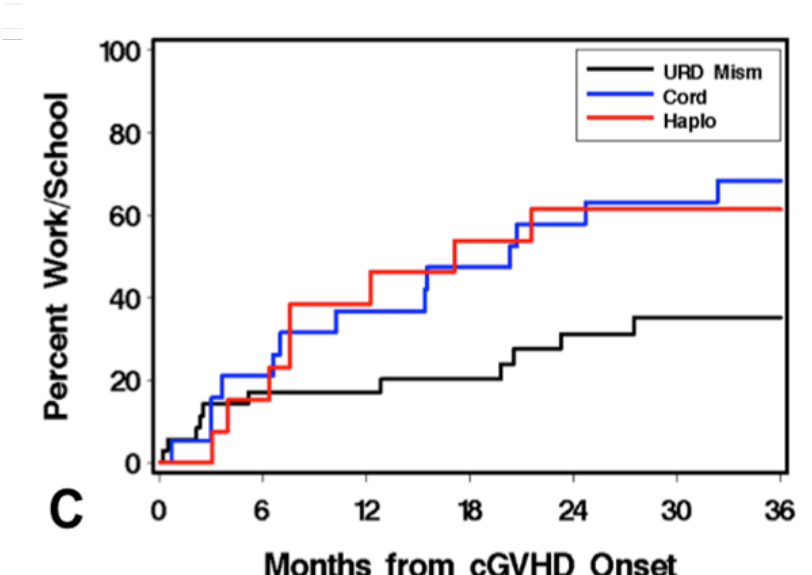

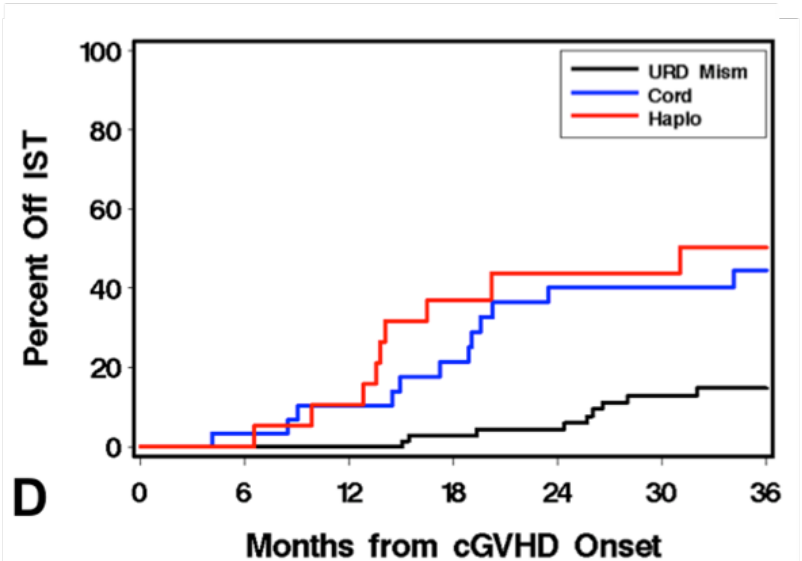

Correlation between grade II-IV aGVHD and cGVHD

	Unrelated Mismatched (N =79)	Cord blood (N = 29)	P[1]	Related Haploidentical (N = 21)	P[2]
Chronic GVHD – no. (%)					
Classic	7 (9)	3 (10)		4 (19)	
Overlap	72 (91)	26 (90)	0.81	17 (81)	0.18
Prior late acute GVHD – no. (%)	14 (18)	3 (10)	0.35	8 (38)	0.05
Prior II-IV acute GVHD –no. (%)	55 (70)	29 (100)	0.0008	20 (95)	0.02
Time from HCT to diagnosis (months), Median (range)	7.8 (2.7-38.2)	3.9 (2.6 -18.2)	0.001	7.5 (2.9-15.4)	0.77

[1] Cord blood vs. mismatched unrelated

[2] Haploidentical vs mismatched unrelated

Late complications and quality of life

Conventional Donor Transplant (BM/PBSC)

- **Lower** risk of early TRM
- **Higher** risk of relapse

Unrelated Donor Transplant Cord Blood

- **Higher** risk of early TRM
- **Lower** risk of relapse

Overall Survival = Overall survival

Late Effects and Patient Reported Quality of Life By Donor Source at 3 Years in Patients Surviving at Least 1 Year Following Hematopoietic Stem Cell Transplantation

Rachel Salit, Filippo Milano and Stephanie Lee

Tandem Meeting 2018

FRED HUTCH
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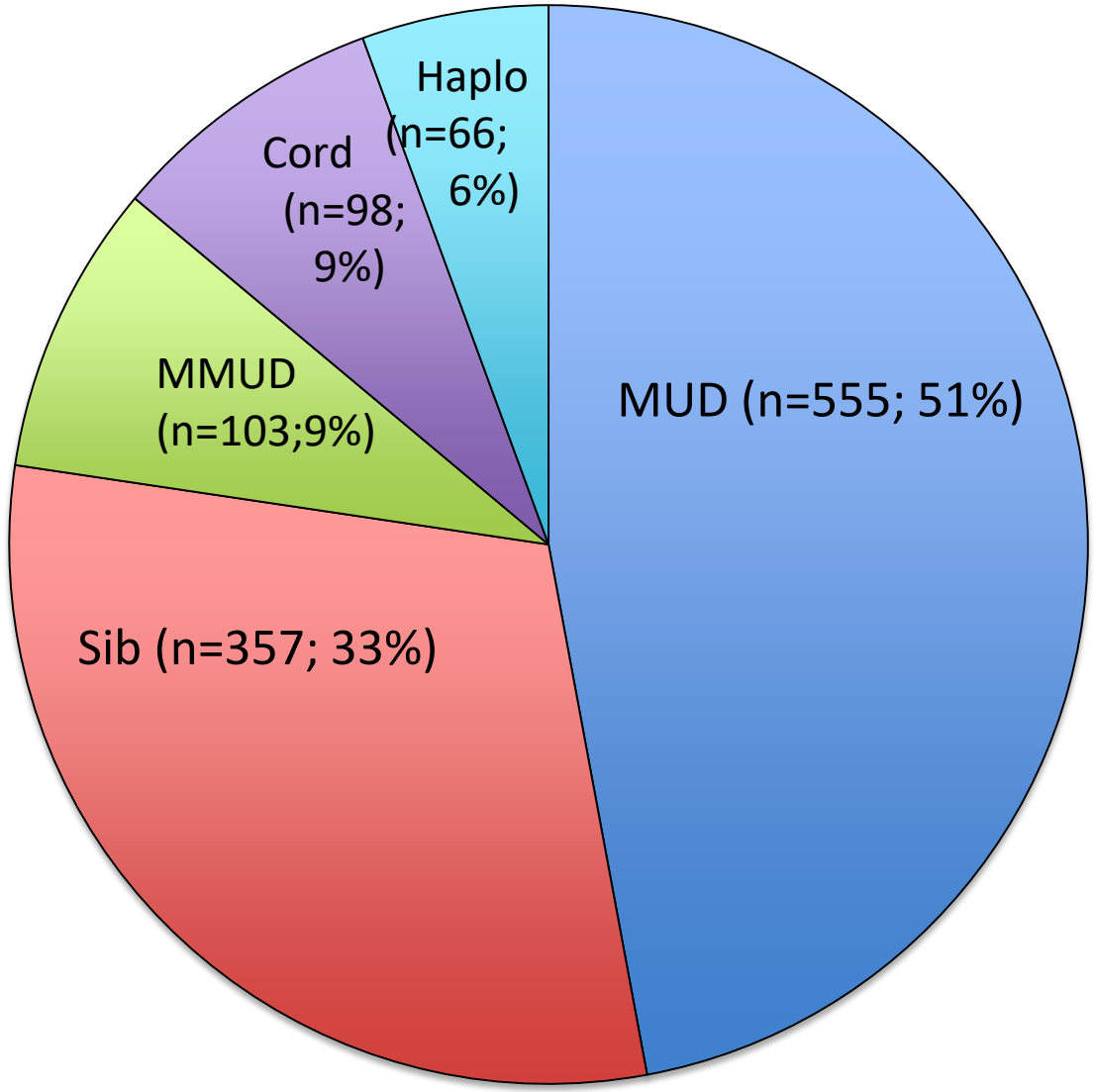
Study Aims

- To describe the incidence of nonmalignant late complications and quality of life amongst recipients of matched related (MRD), 10/10 HLA-matched unrelated (MUD), mismatched unrelated (MMUD), cord blood (UCB), and related haploidentical (Haplo) grafts.

Methods

- 1079 adults who were transplanted between 2008-2016 and survived at least 1 year following transplant.
- Data were derived from review of medical records and annual self-reported questionnaires.
- Only late effects occurring after 1 year were included in this analysis.
- Those occurring between day 100 and 365 were excluded.

Donor cell Distribution at the Hutch



Patient characteristics

	Matched unrelated (n=555)	Matched sibling (n=357)	Mismatched Unrelated (n=103)	Cord blood (n=98)	Haploidentical related (n=66)
Age, years (range)	53 (18-80)	52 (18-79)	55 (21-77)	42 (18-73)	45 (18-68)
Median follow-up in months	43 (12-111)	49 (12-109)	44 (12-109)	40 (13-99)	49 (12-109)
Female	231 (42)	139 (39)	40 (39)	52 (53)	25 (38)
Caucasian	454 (88)	271 (80)	77 (79)	51 (54)	39 (62)
CMV Positive	278 (51)	207 (59)	57 (56)	63 (66)	38 (58)
ALL	76 (14)	42 (12)	10 (10)	24 (24)	4 (6)
AML	197 (36)	107 (30)	30 (29)	45 (46)	15 (23)
CLL	32 (6)	15 (4)	4 (4)	1 (1)	3 (5)
CML	17 (3)	12 (3)	6 (6)	2 (2)	2 (3)
HL	4 (1)	11 (3)	1 (1)	0	16 (24)
NHL	51 (9)	43 (12)	5 (5)	3 (3)	16 (24)
MDS	121 (22)	85 (24)	35 (34)	17 (17)	5 (8)
MM	29 (5)	29 (8)	2 (2)	0	3 (5)

Patient characteristics

	Matched unrelated (n=555)	Matched sibling (n=357)	Mismatched Unrelated (n=103)	Cord blood (n=98)	Haploidentical related (n=66)
BM	54 (10)	27 (8)	7 (7)	0	34 (52)
PBSC	501 (90)	330 (92)	96 (93)	0	32 (48)
Cord	0	0	0	98 (100)	0
MA	345 (62)	224 (63)	62 (60)	77 (79)	14 (21)
NMA	210 (38)	133 (37)	41 (40)	21 (21)	52 (79)
CNI + MMF	267 (48)	176 (49)	45 (44)	97 (99)	0
CNI + MTX	244 (44)	129 (36)	57 (55)	0	5 (8)
Any with post-tx CY	34 (6)	19 (5)	0	0	61 (92)
Other	10 (2)	33 (9)	1 (1)	1 (1)	0

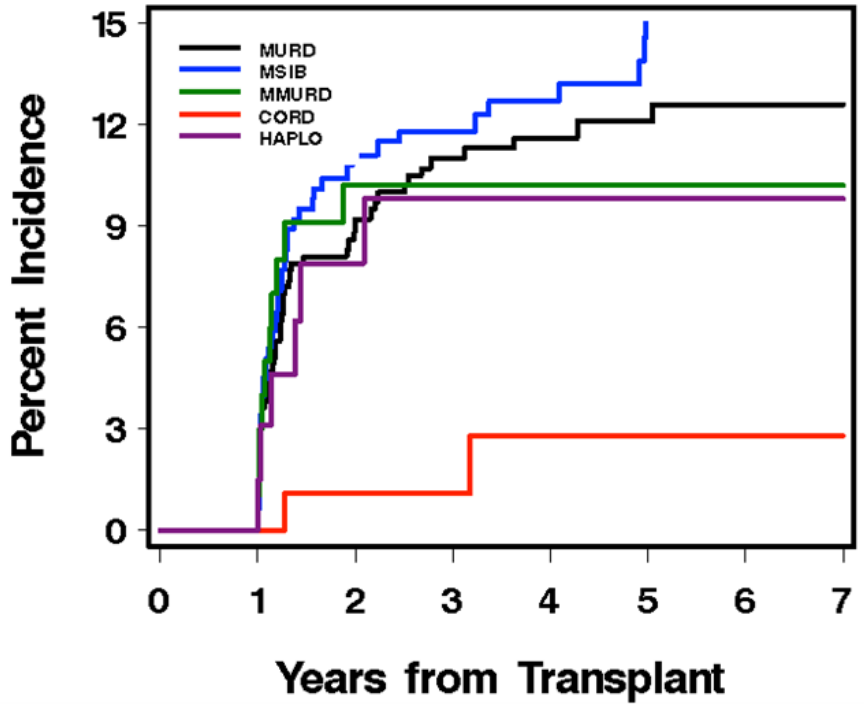
Non-malignant late effects

47 non-malignant late effects were divided into 9 categories:

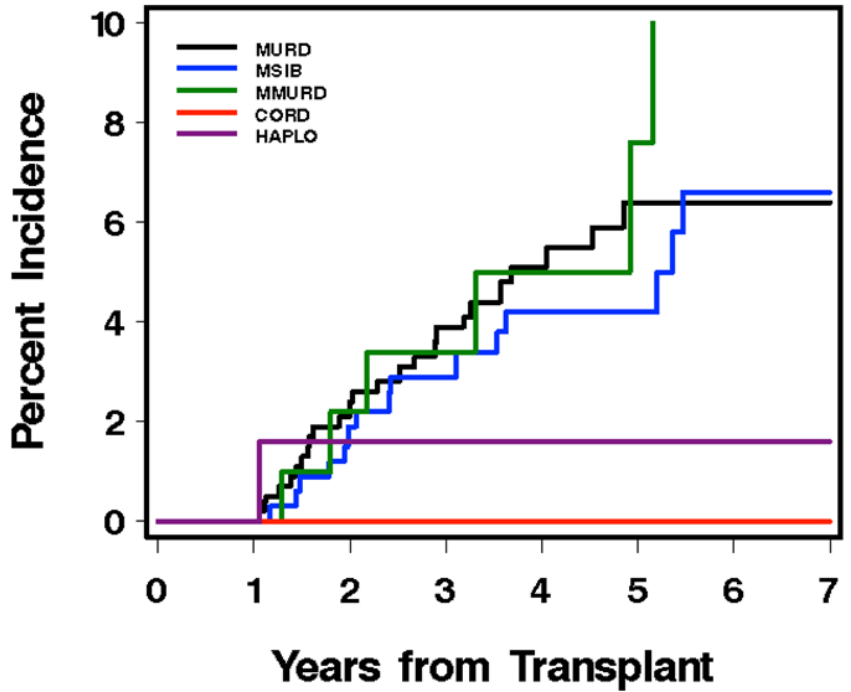
- Bone loss
- Psychological issues
- Cardiac
- Orthopedic
- Pulmonary
- Hypogonadism
- Systemic viral infection
- Respiratory virus infection
- Unusual infections

Cumulative incidence of late effects

Bone loss



Cardiac Events



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QQL-PDQ Results

- By patient-reported questionnaire (45% response, median follow up 35 months), there was no difference in:

- Physical and mental functioning as measured by the SF-36
- Self-reported Karnofsky scores between the 5 groups.

- CB and Haplo recipients were less likely to report taking steroids for chronic GVHD ($p < 0.0001$)

Conventional Donor Transplant (BM/PBSC)

- **Lower** risk of early TRM
- **Higher** risk of relapse

Unrelated Donor Transplant Cord Blood

- **Higher** risk of early TRM
- **Lower** risk of relapse
- **Better** outcomes in patients with MRD
- **Lower** rate of cGVHD
- **Higher** chance of returning work/school
- **Lower** long-term complications (bone and cardiac)

Overall Survival ≠ Overall survival (improved)

Acknowledgments

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Nurses, Physicians Assistant, Nurse Practitioners, Pharmacists

Patients
Colleen Delaney

Cord blood Group

Thank you!

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