

# **Double unrelated umbilical cord blood versus HLA-haploidentical bone marrow transplantation (BMT CTN 1101)**

(NCT 01597778)

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On behalf of the Blood and Marrow Transplant Clinical Trials Network

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# Conflict of interest

Research funding: GamidaCell, Magenta, Astex, FateTherapeutics

Advisory Board: AlloVir

# Hypothesis

**As compared to dUCB, haplo-BM would have a 15% higher 2-year PFS.**

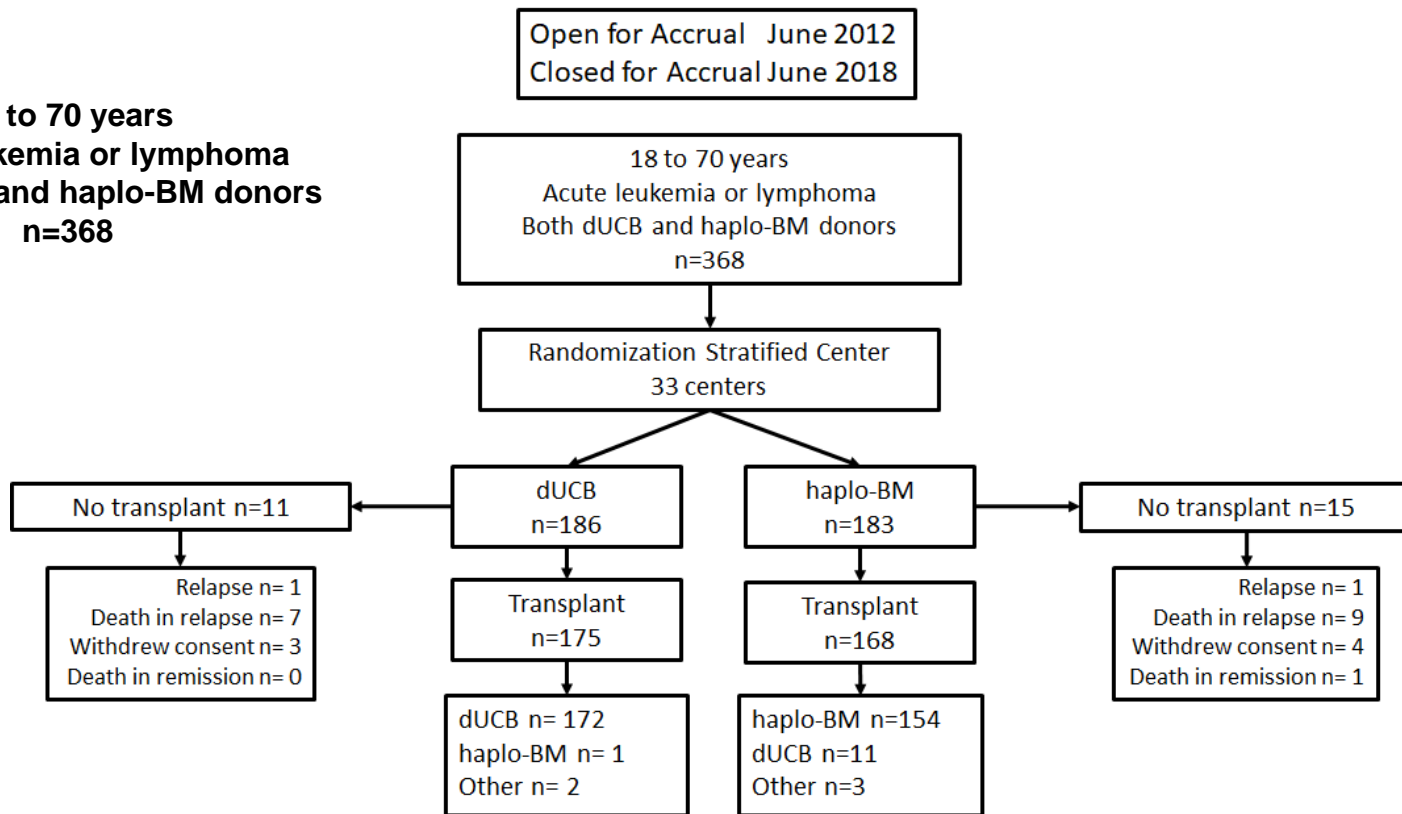
- **Null hypothesis: no difference in 2-year PFS between treatment arms**
- **Target sample size of 205 per group to maintain type I error of 5% while providing 80% statistical power for a two-sided test to detect a 15% increase in 2-year PFS in haplo-BM arm**

# Study Design

- **Phase III, randomized trial of RIC: dUCB versus haplo-BM**
- **Hematologic malignancy (acute leukemia / lymphoma)**
- **Primary endpoint: progression-free survival at 2 years**
- **Intent-to-treat analysis from time of randomization**

# Accrual

**18 to 70 years**  
**Acute leukemia or lymphoma**  
**Both dUCB and haplo-BM donors**  
**n=368**



# Characteristics: Acute Leukemia

	dUCB N = 186	haplo-BM N = 182
Disease status: 1 <sup>st</sup> complete remission	74%	85%
Disease status: 2 <sup>nd</sup> complete remission	26%	15%
Disease status: ≥3 <sup>rd</sup> complete remission	—	<1%
Cytogenetic risk	-	-
Cytogenetic risk Favorable	13%	15%
Cytogenetic risk Intermediate	46%	41%
Cytogenetic risk Poor	32%	33%
Cytogenetic risk Not reported	10%	12%

# Characteristics: Lymphoma

Disease status	dUCB N = 186	haplo-BM N = 182
Complete response	39%	32%
Partial response	48%	57%
Follicular or other non-Hodgkin	14%	11%

# Graft Characteristics

	dUCB N=175	haplo-BM N=167
TNC infused, median, IQR	2.95 (1.85 – 4.32) x 10 <sup>7</sup> /kg	2.68 (1.87 – 3.63) x 10 <sup>8</sup> /kg
CD34 infused, median, IQR	1.30 (0.70 – 2.30) x 10 <sup>5</sup> /kg	2.87 (1.44 – 3.86) x 10 <sup>6</sup> /kg
CD3 infused, median, IQR	5.50 (1.90 – 8.20) x 10 <sup>6</sup> /kg	2.96 (2.24 – 4.28) x 10 <sup>7</sup> /kg



# Results by Intention-to-treat

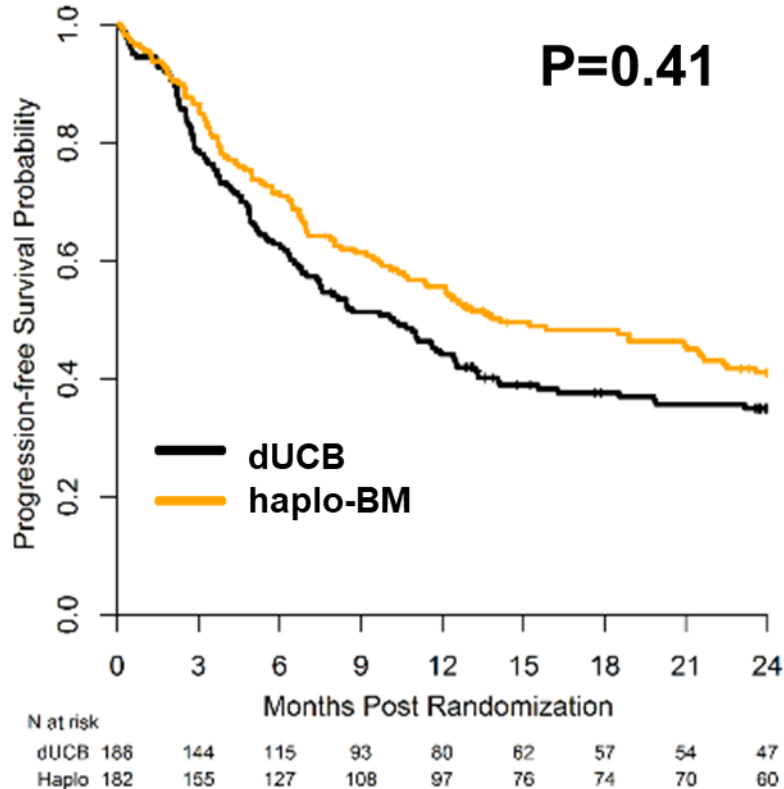
## from the time of randomization:

- Progression-free-survival
- Treatment-related mortality
- Relapse/Progression
- Overall survival

## by treatment arm:

- Neutrophil recovery
- Platelet recovery
- Acute GVHD
- Chronic GVHD

# Primary Endpoint –Progression-Free Survival at 2 yrs.



Intention-to-treat	dUCB	haplo-BM
Number of events	117	104
PFS at 2 yrs.	35%	41%
95% Conf. interval	28%-42%	34%-48%
Median follow-up	25 months	25 months
Range	20-26 months	23-25 months

**$\Delta=6.1%$  (95%CI -5% to 17%)**

# Multivariate Analysis: Progression-free Survival

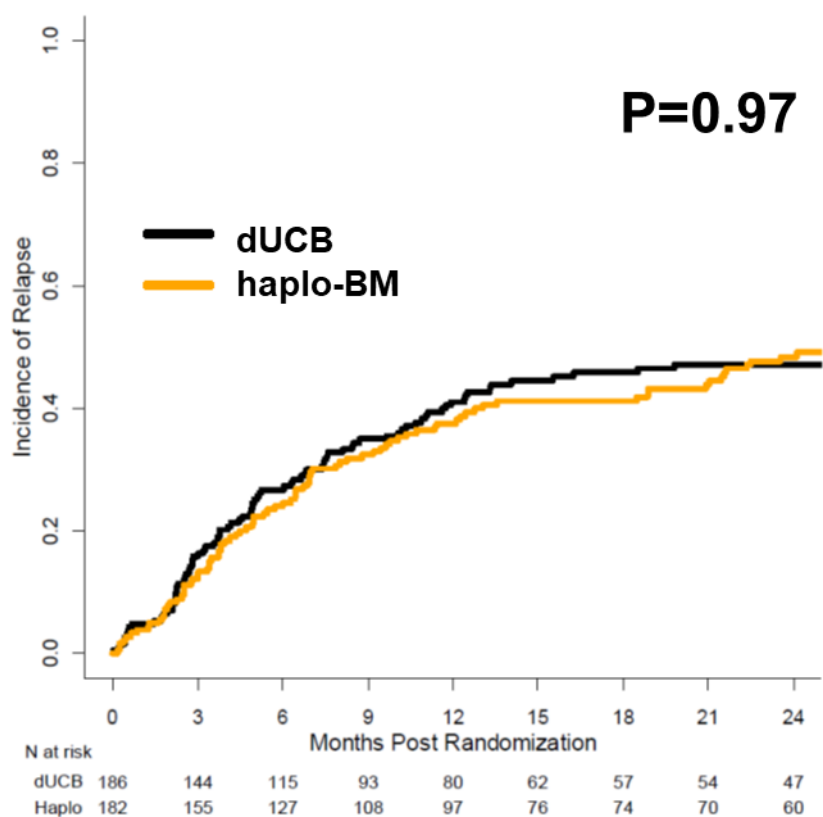
	Hazard Ratio (95% confidence interval)	P-value
Donor	-	0.060
haplo-BM	1.00	-
dUCB	1.30 (0.99 – 1.70)	0.060

	Hazard Ratio (95% confidence interval)	P-value
Adjusted for transplant center	-	-
Donor	-	-
Haplo-BM	1.00	
dUCB	1.27 (0.92-1.75)	0.162

## Multivariate Analysis: Progression-free Survival

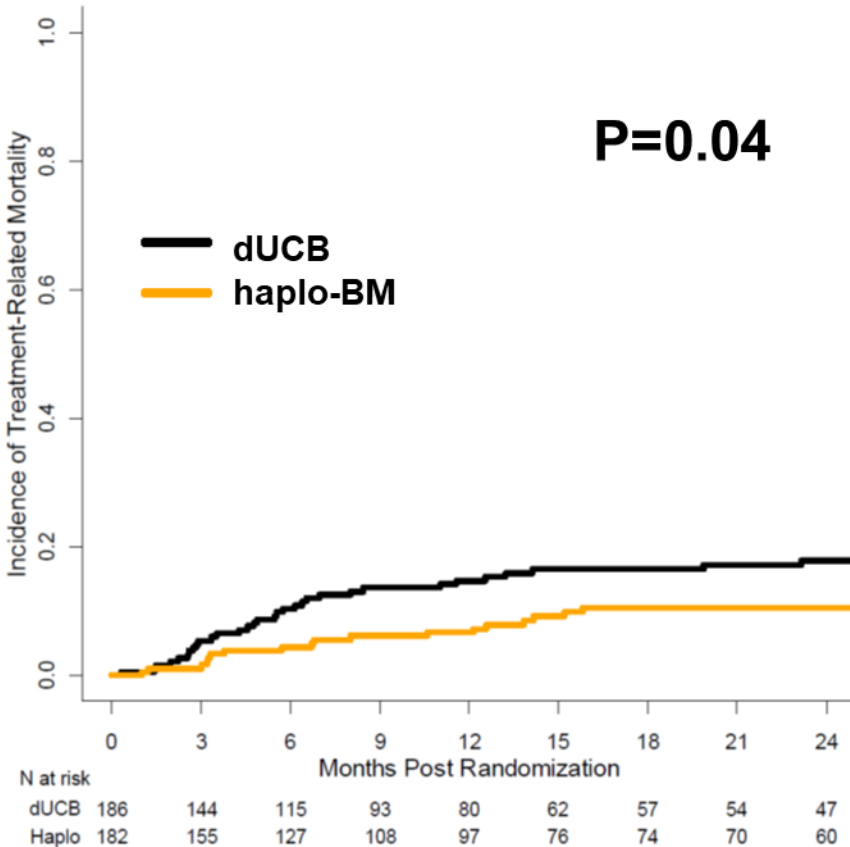
	Hazard Ratio (95% confidence interval)	P-value
Disease Risk	-	0.029
Acute leukemia, CR 1	1.00	-
Acute leukemia, CR 2 and CR 3	0.91 (0.62 – 1.34)	0.64
Lymphoma, CR	0.58 (0.34 – 1.01)	0.053
Lymphoma, PR	1.51 (1.04 – 2.20)	0.032
Follicular lymphoma	0.82 (0.38 – 1.78)	0.621
Age, >59 years at randomization	1.00 (0.76 – 1.32)	0.979
Performance score, 90 – 100	1.05 (0.79 – 1.40)	0.742

# Cumulative Incidence of Relapse at 2 yrs.



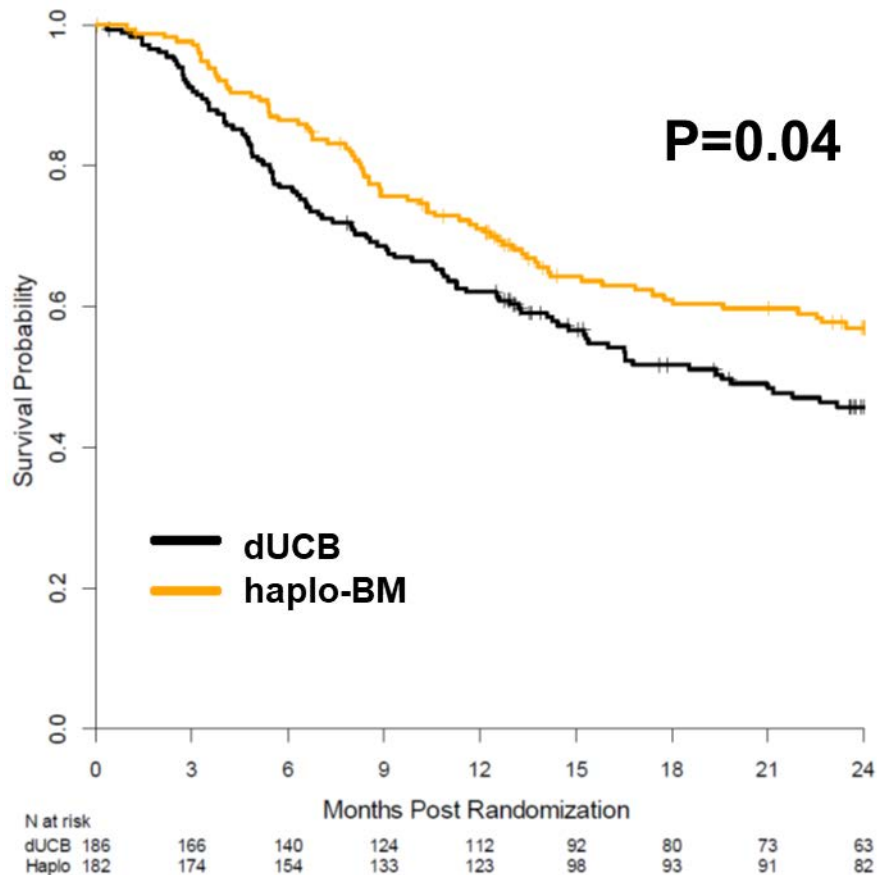
Intention-to-treat	dUCB	haplo-BM
Relapse at 2 yrs.	47%	48%
95% Conf. interval	40%-54%	41%-56%

# Cumulative Incidence of TRM at 2 yrs.



Intention-to-treat	dUCB	haplo-BM
TRM at 2 yrs.	18%	11%
95% Conf. interval	13%-24%	7%-16%

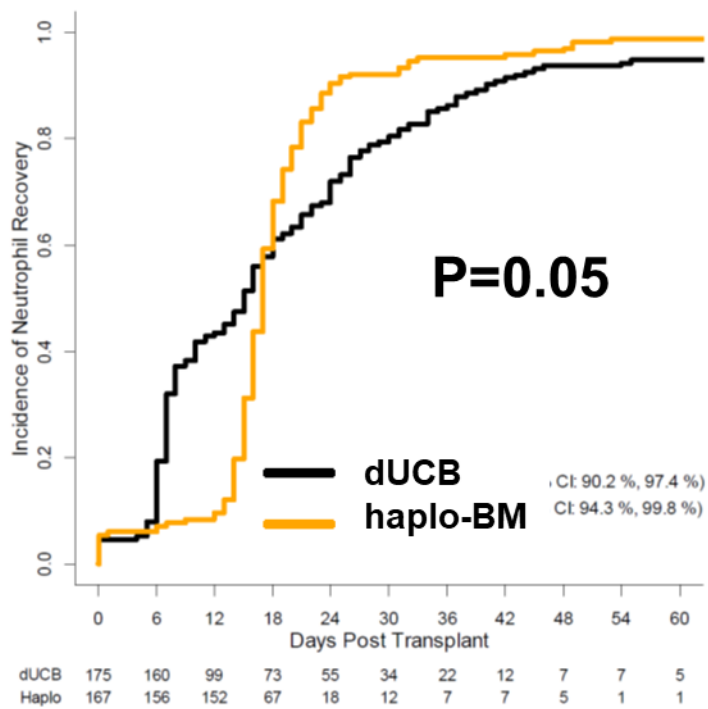
# Overall Survival at 2 yrs.



Intention-to-treat	dUCB	haplo-BM
Number of events	117	104
OS at 2 yrs.	46%	57%
95% Conf. interval	38%-53%	49%-64%

Main COD	dUCB	haplo-BM
Primary disease	55	46
Infections	16	13
Organ failure	14	8

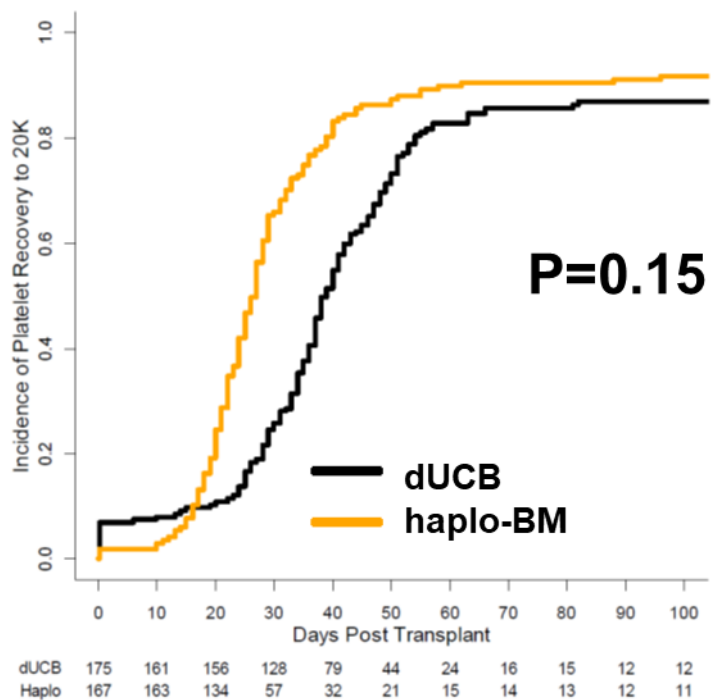
# Neutrophil Recovery by Treatment Arm



By treatment arm	dUCB	haplo-BM
Number of patients	175	167
Anc > 500	95%	99%
95% Conf. interval	90%-97%	94%-100%
Median in days	15 (r: 4-69)	17 (r:1-87)

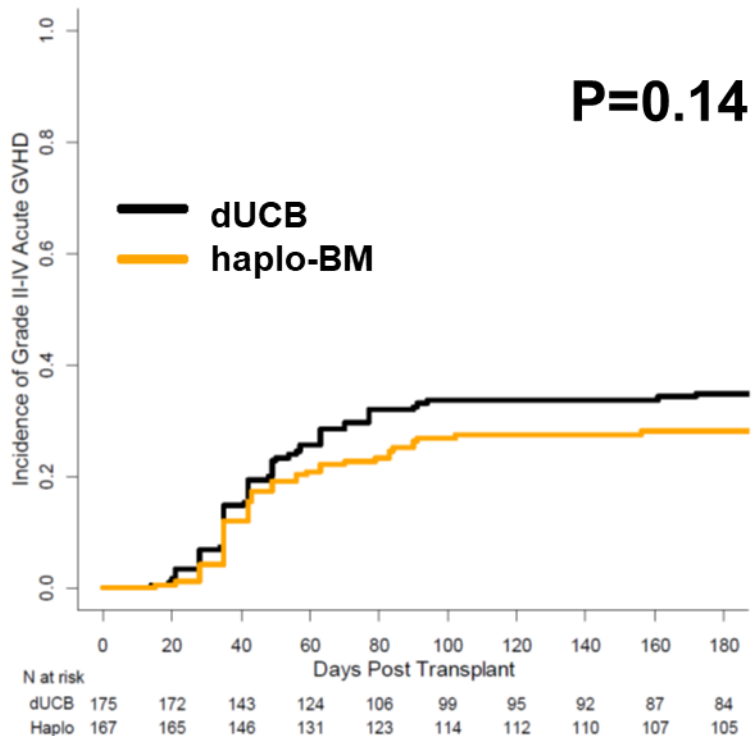


# Platelet Recovery > 20K by Treatment Arm



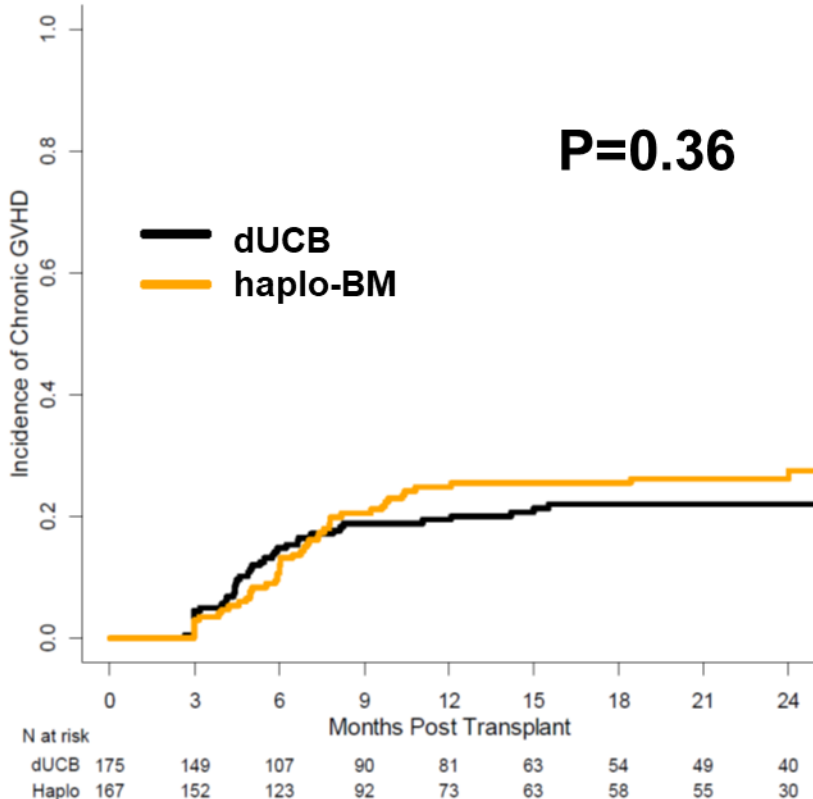
By treatment arm	dUCB	haplo-BM
Number of patients	175	167
PLT > 20K at 100days	78%	84%
95% Conf. interval	71%-84%	78%-89%
Median in days	42 (r: 7-147)	28 (r: 12-173)

# Grades II-IV Acute GVHD at day +180 by Treatment Arm



By treatment arm	dUCB	haplo-BM
Number of patients	175	167
aGVHD at 180 days	35%	28%
95% Conf. interval	28%-42%	22%-35%
Grades III-IV	9%	7%
95% Conf. interval	5%-13%	4%-12%

# Chronic GVHD at 2 yrs. by Treatment Arm



By treatment arm	dUCB	haplo-BM
Number of patients	175	167
cGVHD at 2 yrs.	22%	26%
95% Conf. interval	16%-29%	20%-33%

# Summary

**No significant difference in PFS at 2-years between dUCB and haplo-BM with or without adjustment for transplant center.**

**Neutrophil recovery was faster in dUCB but higher incidence by day +60 in haplo-BM.**

**TRM was lower and survival was higher in haplo-BM.**

**There were no significant differences in relapse, grade II-IV or III-IV acute GVHD, and chronic GVHD.**

# Conclusion

**Among the 368 patients randomized on this study, no significant difference was observed in the 2-year PFS between the dUCB and haplo-BM arms suggesting both donor types extend access to transplantation.**

**Although the trial did not record the expected 15% difference in 2-year PFS between treatment arms in adults with hematologic malignancy, lower NRM and higher overall survival favor haplo-BM transplantation.**

# However

**Taking a closer look into the data...**

# CTN 1101 vs. The Community

## Research hypothesis:

- Outcomes from a contemporary registry study will approximate outcomes from a phase III randomized clinical trial

## Endpoints:

- Primary endpoint: Progression-free survival at 2-yr post-transplant
- Secondary endpoints: hematopoietic recovery, graft failure, acute and chronic GvHD, relapse, non-relapse mortality and overall survival

# CTN 1101 vs. The Community

	CTN1101		Non-CTN1101		
Donor Type	BM	dUCB	BM	PB	dUCB
No. of patients	157	185	319	409	147
No. of centers	29	31	40	73	38

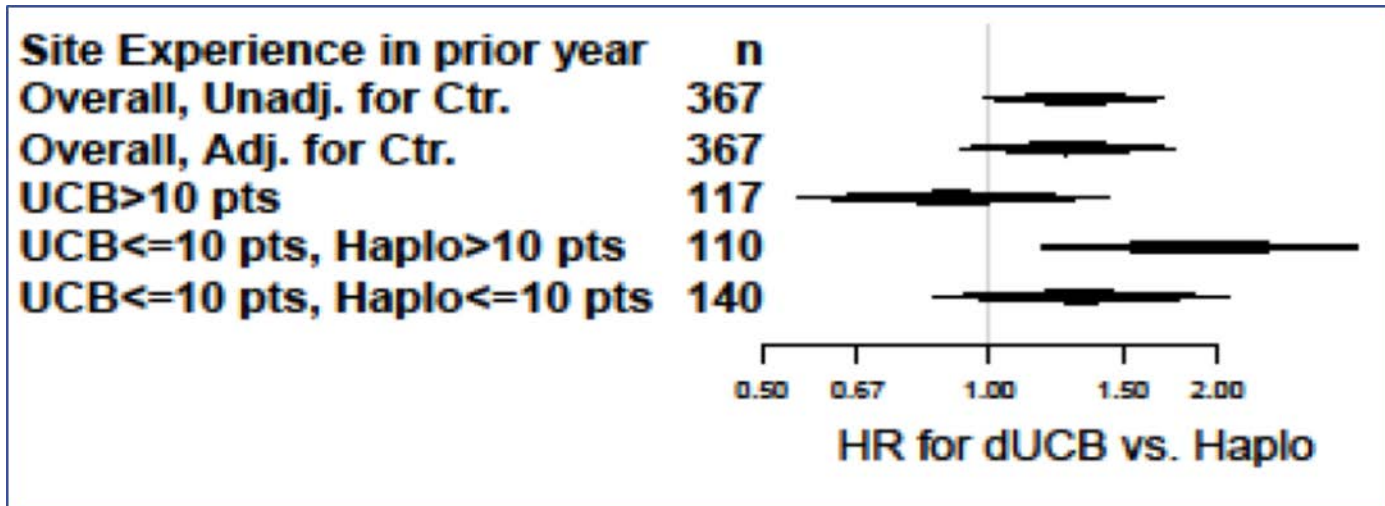


# Effect of Center Expertise

Progression-Free Survival	Hazard Ratio (95% confidence interval)	P-value
Adjusted for transplant center Haplo-BM	1.00	
Adjusted for transplant center dUCB	1.27 (0.92-1.75)	0.162

# Effect of Center Expertise

Center experience with Haplo and dUCB		
>10 UCB transplants	<=10 UCB transplants >10 haplo transplants	<=10 UCB transplants <=10 haplo transplants
(n=117, 10 centers)	(n=110, 2 centers)	(n=140, 21 centers)



# CTN 1101 Quality of Life

FACT-BMT: The Functional Assessment of Cancer Therapy – Bone Marrow Transplant subscale version 4.0 instrument: Physical Well-being, Social/Family Well-being, Emotional Wellbeing, and Functional Well-being.

MOS SF-36: The Medical Outcomes Study Short Form 36. Physical Functioning, Role Physical, Pain Index, General Health Perceptions, Vitality, Social Functioning, Role Emotional, and Mental Health Index.

Global HQL: Four standard questions to assessed patient self-assessed Karnofsky performance status, overall health and overall quality of life, (excellent, very good, good, fair, poor).

Occupational Functioning: Occupational functioning assessed current job status, type of work, number of hours of paid and unpaid work, school, importance of work and change in work goals.

EQ-5D: The EQ-5D collected data used to calculate patient-reported utilities for cost-utility analyses and contains a five item survey measuring mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

# Cost Effectiveness Analysis

PI Scott Ramsey

- Single center studies suggested that early post-HCT cost after dUCB to be higher than haplo-BM
- Hypothesis: haplo-BM more cost effective than dUCB
- Plan: obtain 2-year cost data in CTN 1101 patients
- “Glitch”: insurance companies declined to provide data
- Solution: to cross reference Vizient and CIBMTR data

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# Acknowledgements



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and Blood Institute



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BLOOD AND MARROW  
**TRANSPLANT**  
CLINICAL TRIALS NETWORK

**Patients & Families**

**BMT CTN Co-  
investigators &  
Transplant Centers**



**Emmes**