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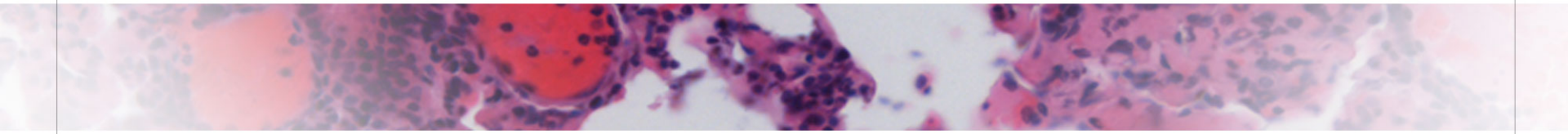


NiCord Single Unit Expanded Umbilical Cord Blood Transplantation: Final Results of a Multicenter Phase I/ II Trial

Mitchell E. Horwitz, MD
Duke University Medical Center
Durham, NC

Gamida Cell
Jerusalem, Israel

Guillermo Sanz, MD
Hospital Universitario y Politécnico La Fe
Valencia Spain

Umbilical Cord Blood Stem Cell Grafts

- Advantages
  - Readily available stem cells source
  - Tolerance across HLA barriers
  - Nearly 30 year of experience
  - Less chronic GvHD vs. Matched Unrelated donor
    - *Eapen M et al Lancet 2010*
  - Potent anti-tumor activity
    - *Milano F et al NEJM 2016*
- Disadvantages
  - Low stem cell dose
    - Delayed hematopoietic recovery
    - Delayed immunologic recovery
  - Increased resource utilization

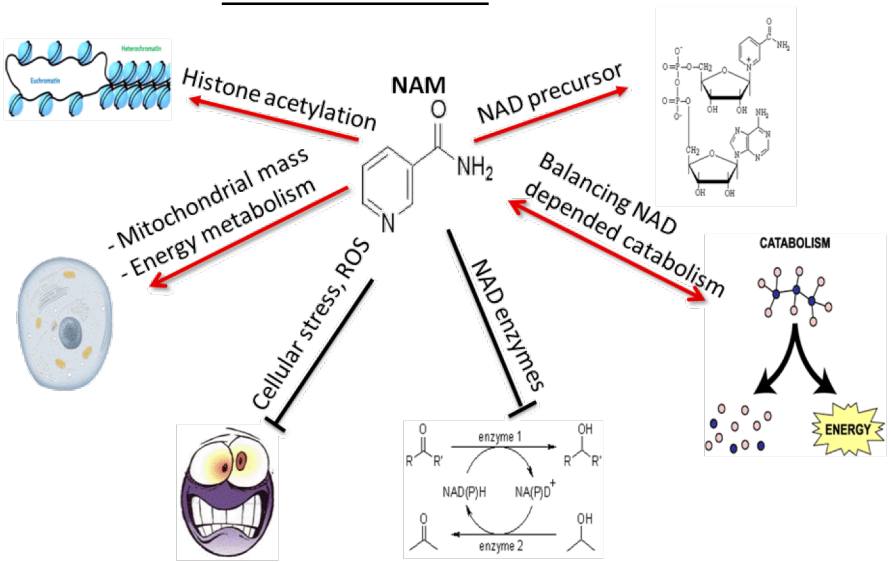
Potential Solution

Ex-vivo Expansion Cord Blood Stem Cells

NiCord Stem Cell Expansion Technology

- An ex vivo expanded cell product derived from a umbilical cord blood
- Developed in the laboratories of Gamida Cell Ltd.
- Culture system: Nicotinamide + TPO, IL-6, FLT-3 ligand and SCF

Nicotinamide



Affect on CD34+ Stem Cells

- Preserves gene expression profile similar to non-cultured cells
- Modulates cellular metabolism and transport related genes
- Increase in stress resistance
- Increase in stem cell engraftment efficiency

Pilot Trial: NiCord + Unmanipulated Double Cord Blood Transplantation

- 11 patients, myeloablative conditioning (2010-2012)
- NiCord expanded graft + Unmanipulated cord blood graft
- NiCord engraftment dominant in 8 of 11 recipients
- Shortened time to hematopoietic recovery (compared to historical controls)
  - Neutrophils >500 (mean days): 25 ➔11
  - Platelets > 20K (mean days): 41➔31
  - 3 year overall survival: 67%
  - 3 year progression-free survival: 67%
- NiCord derived hematopoiesis stable and robust
  - Median f/u 6yrs (range 5-7 years)

Patrick Stiff, MD Loyola University, Chicago

Horwitz et al. JCI 2014

Can NiCord be used as a single, stand-alone graft?

Phase I/II Multicenter Study of NiCord as a Stand-alone Graft

Primary Objective

1. To assess the cumulative incidence neutrophil engraftment at 42

Design

- 12-65 years old
- AML, ALL, MDS, CML, Lymphoma
- Myeloablative Conditioning regimen;
  - Regimen A: TBI 1350cGy, Fludarabine and Cyclophosphamide/Thiotepa
  - Regimen B: Thiotepa, Busulfan, Fludarabine
  - Regimen C: Clofarabine, Fludarabine, Busulfan
- GvHD prophylaxis
  - Mycophenolate mofetil, Tacrolimus or cyclosporine
- 13 sites: US, EU, Asia

Protocol Schema

NiCord Unit

Shipped to Centralized Manufacturing facility

CD 133+ Cell Selection

CD133 Negative Fraction

Non-cultured fraction (NF)

Lymphocyte Containing Cryopreserved

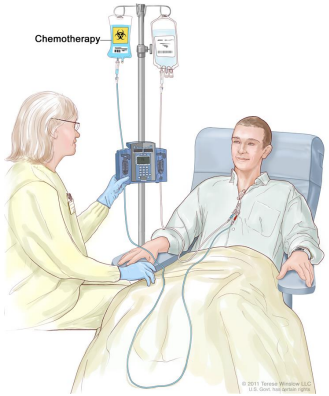
+

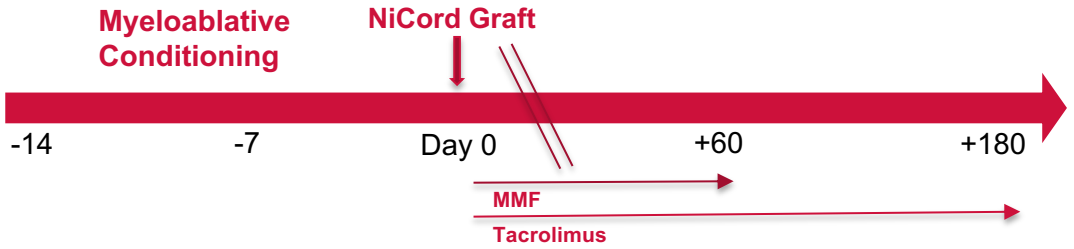
CD133+ Fraction

Cultured fraction (CF)

Cultured 21±2d in cytokines + Nicotinamide Transported Frozen to Site

NiCord Graft





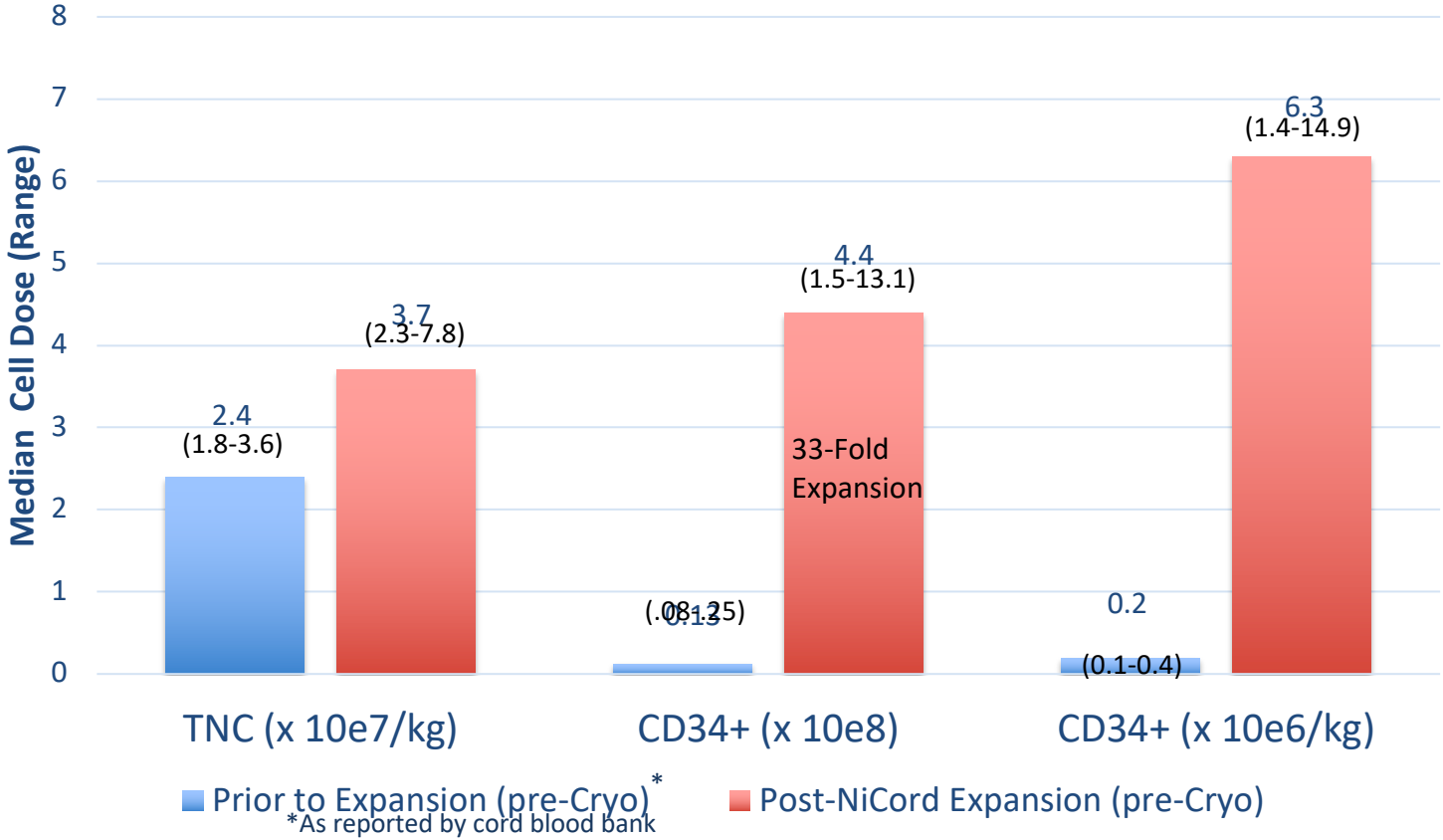
Demographic and Baseline Characteristics

		NiCord N (%)
Number of evaluable patients		**36 (100)**
Age (years)	13-18	4 (11)
	19-39	11 (31)
	40 +	21 (58)
	Median	**44**
	(range)	**(13-63)**
HLA Match Score	4/6	26 (72)
	5/6	8 (22)
	6/6	2 (6)
Conditioning Regimen	Regimen A (TBI, Fludarabine +/- Cy or Thiotepa)	15 (42)
	Regimen B (Thiotepa, Busulfan, Fludarabine)	19 (53)
	Regimen C (Clofarabine, Fludarabine, Busulfan)	2 (6)
Weight (Kg)	***Median***	75
	(range)	(41-125)

Demographic and Other Baseline Characteristics

		NiCord N (%)
Primary Diagnosis	**Acute Lymphoblastic Leukemia**	**9 (25)**
	High risk first complete morphologic remission (CR1)	5
	Second Remission	4
	Acute Myelogenous Leukemia	**17 (47)**
	First complete morphologic remission (CR1)	13
	Second Remission	4
	Myelodysplastic Syndrome	
	Chronic Myelogenous Leukemia	**7 (19)**
	Hodgkin's Disease	**2 (6)**
		1 (3)
Disease Risk	**Low**	
	Intermediate	**8 (22)**
	High	**15 (42)**
		13 (36)

Graft Characteristics

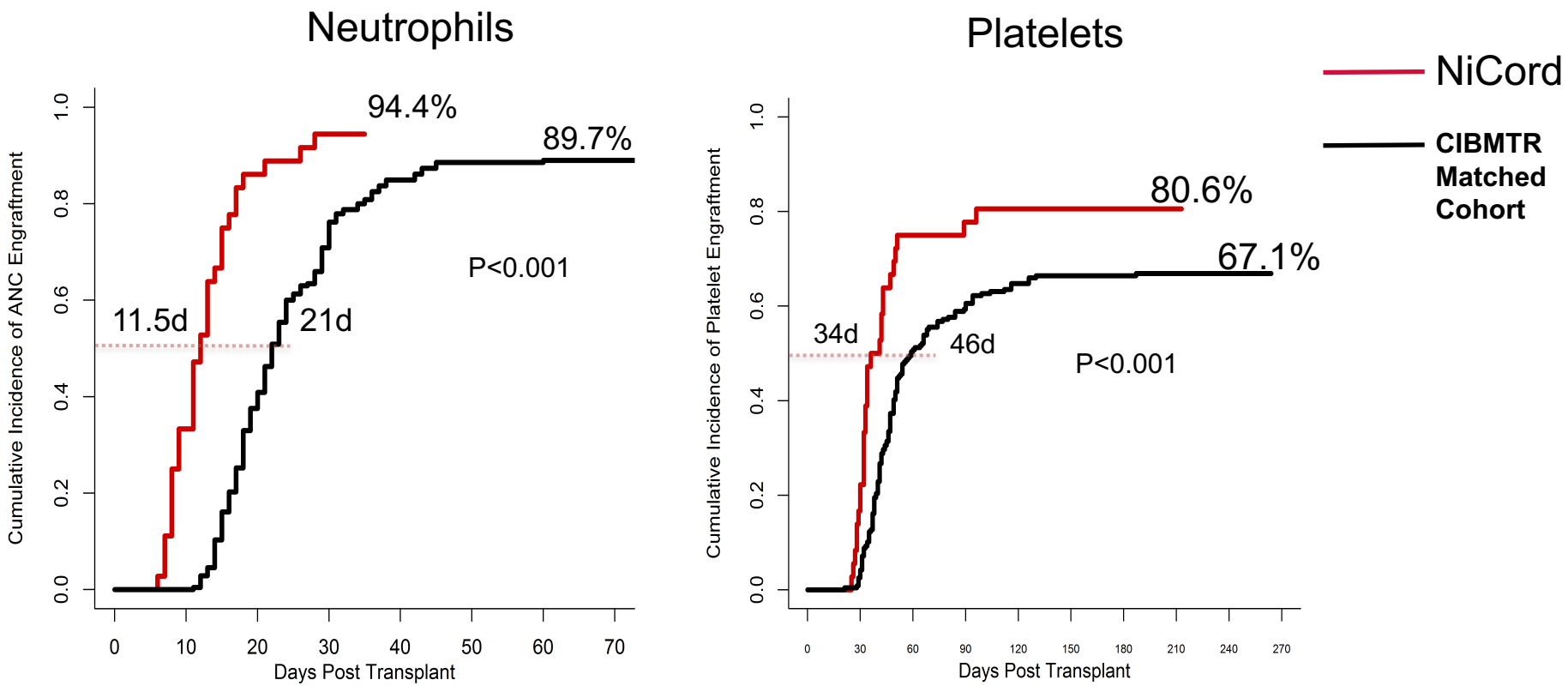


Standard Myeloablative Umbilical Cord Blood Transplantation CIBMTR Matched Control Cohort

Selection Criteria Applied Sequentially	Number of Matching Patients
CBU transplants from 2010 to 2013*	1037
Age 13-63	820
Myeloablative conditioning	519
Disease status similar to NiCord patients	371
Cell count criteria	184
HLA match criteria	153
Performance score criteria	146
Final sample size	146

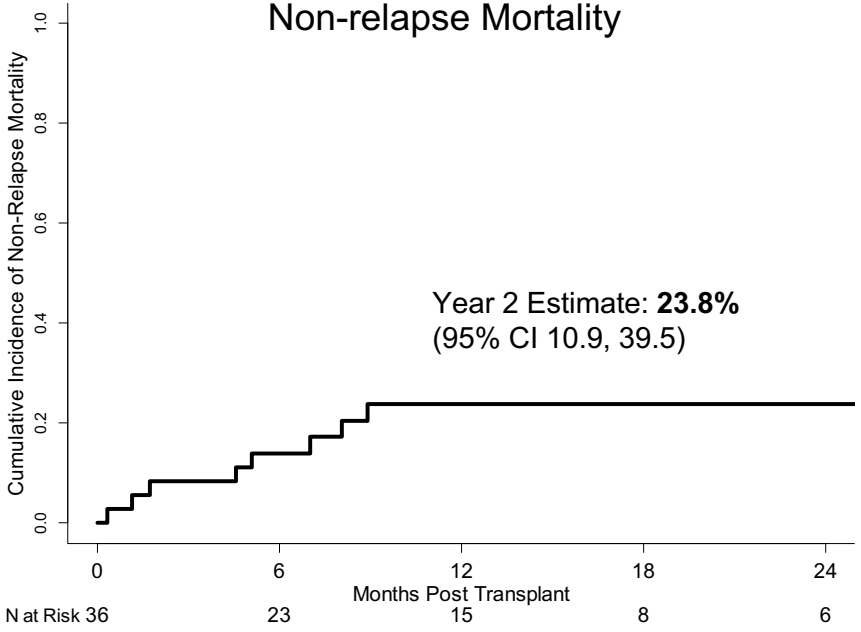
*Double Cord-80% Single Cord-20%

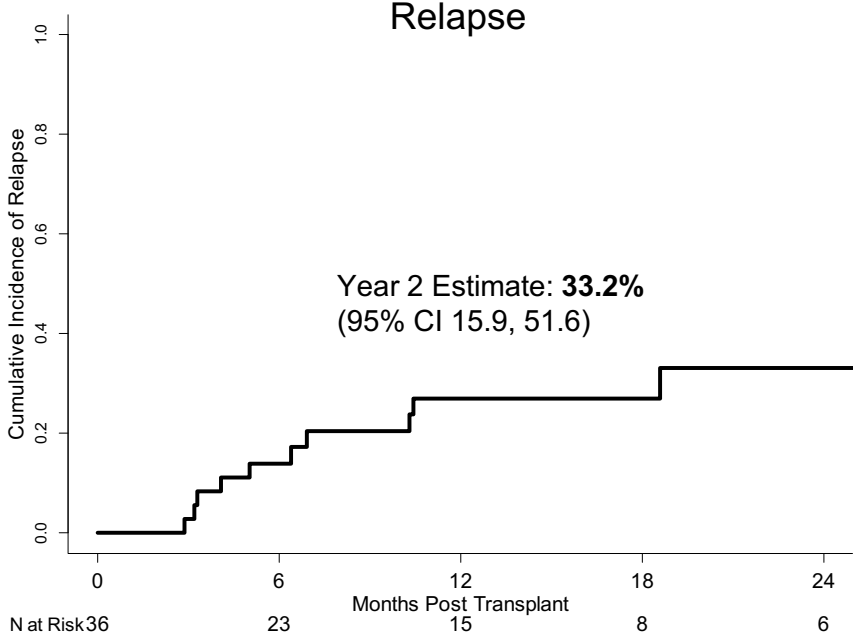
Engraftment; NiCord vs. CIBMTR Matched Control



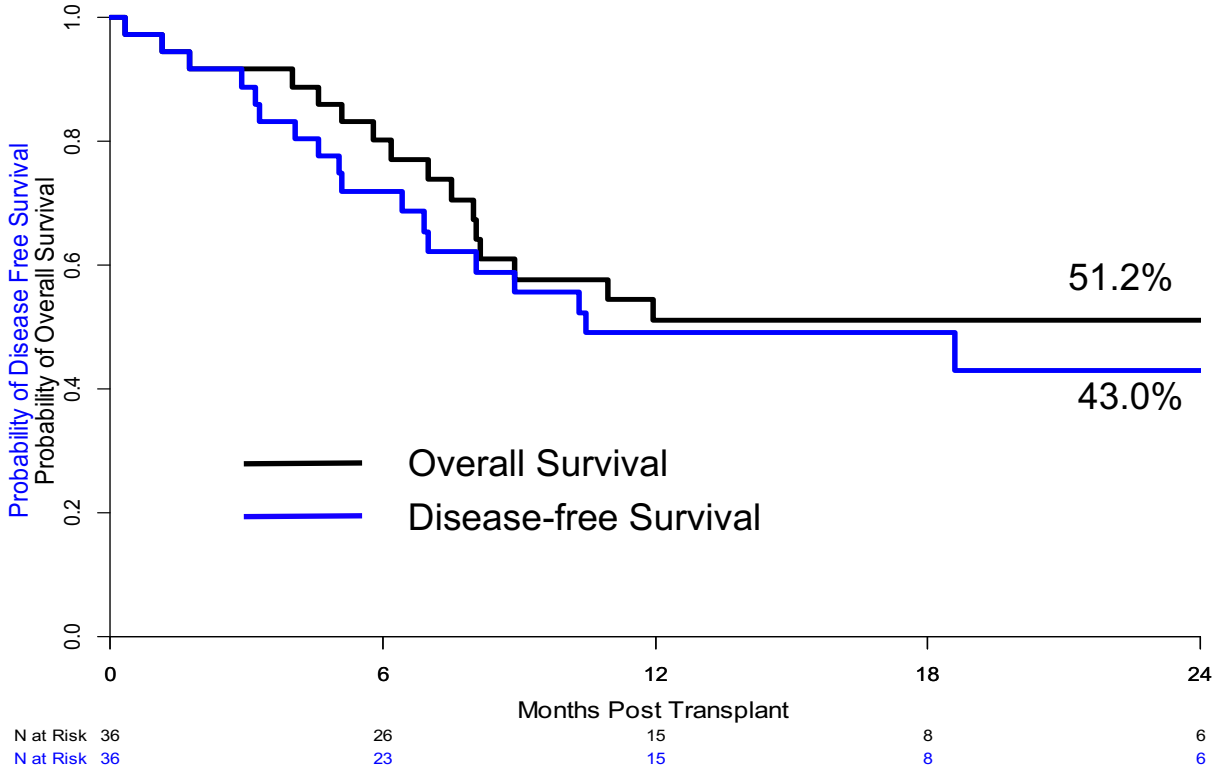
The data presented here include data obtained from the Center for International Blood and Marrow Transplant Research.

NiCord Phase I/II Outcome





NiCord Phase I/II Outcome: Disease-free and Overall Survival

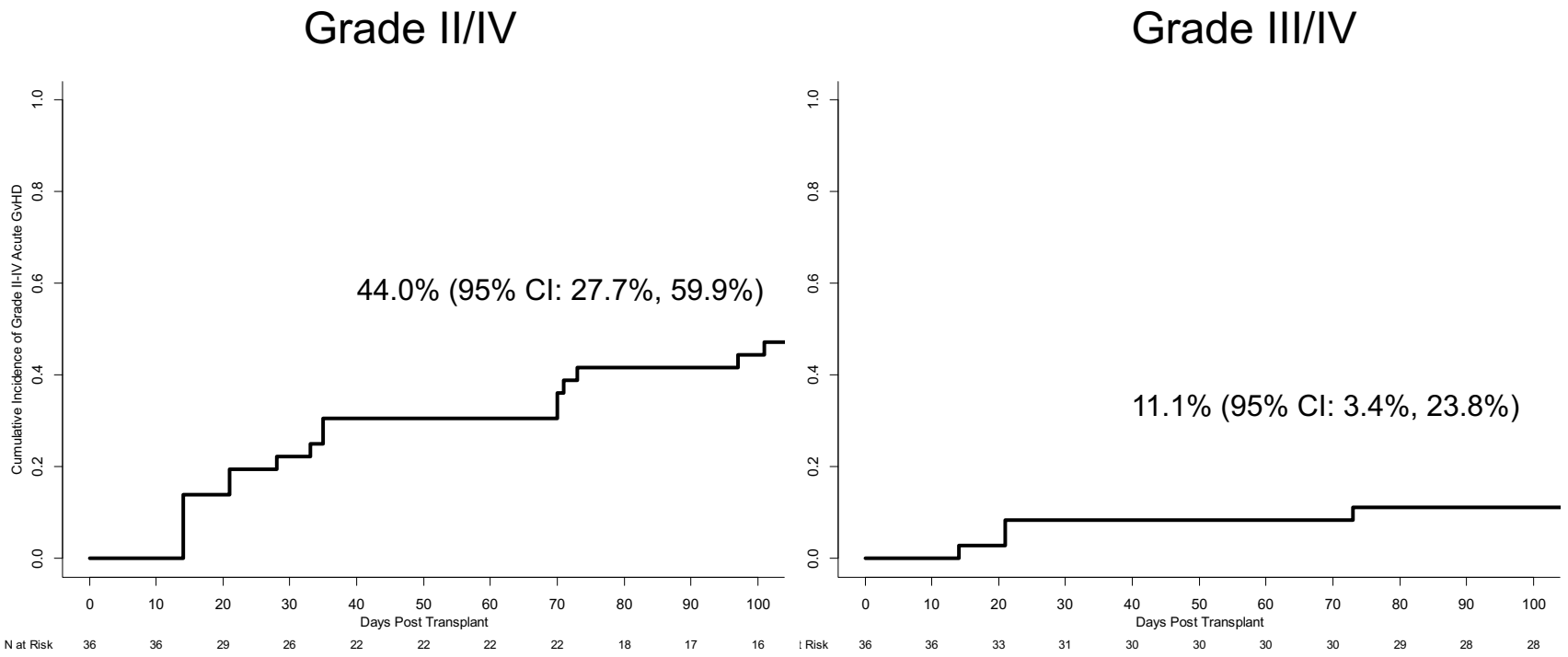


Estimated Disease-Free Survival
1yr: 49.1% (95% CI 32.2%, 64.8%)
2yr: 43.0% (95% CI 24.2%, 60.5%)

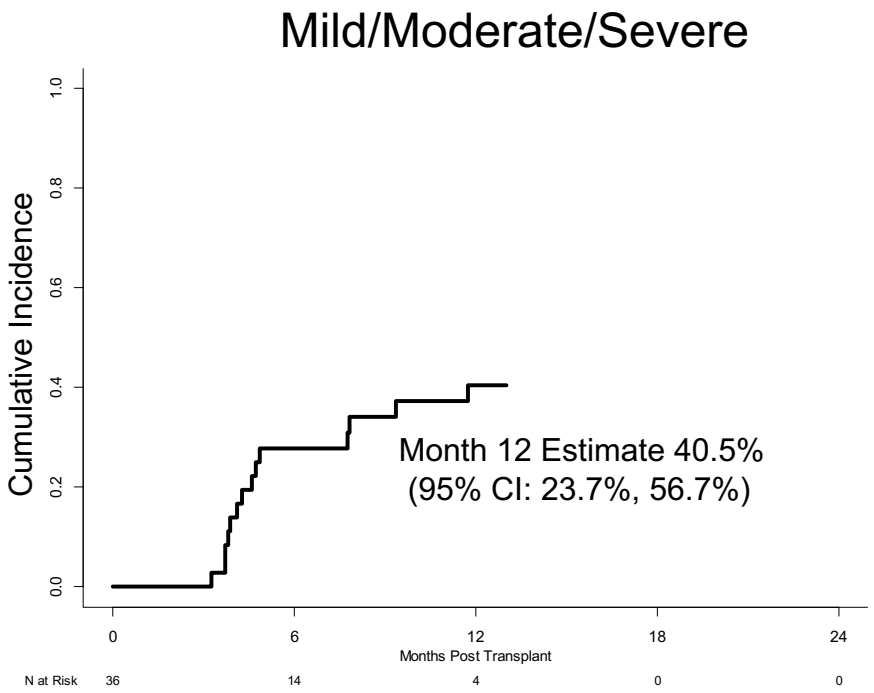
Estimated Overall Survival
1yr: 51.2% (95% CI 32.9%, 66.8%)
2yr: 51.2% (95% CI 32.9%, 66.8%)

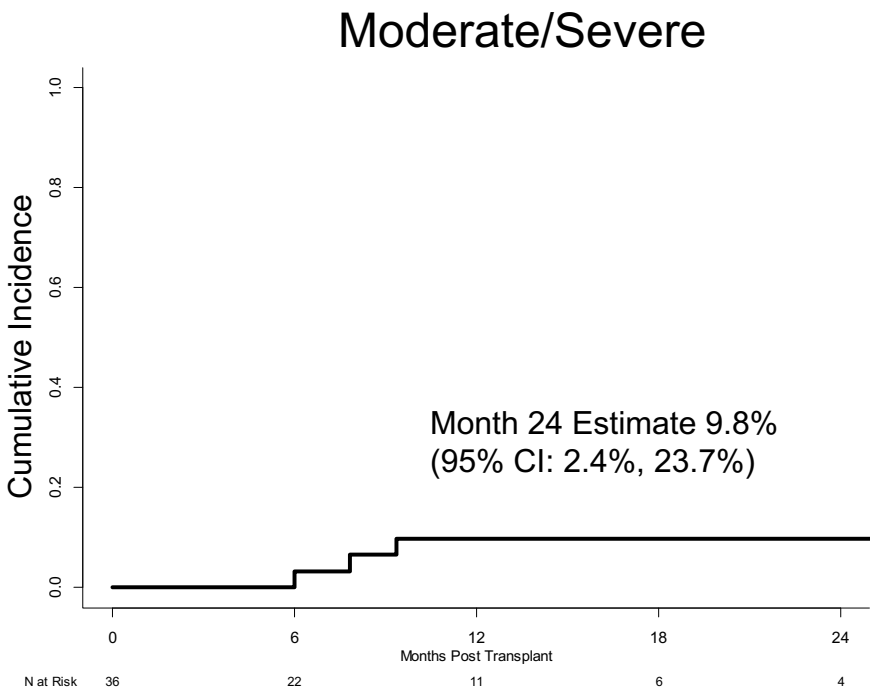
Median Follow-up (survivors); 14 month (5-37months)

NiCord Phase I/II; Acute Graft vs. Host Disease

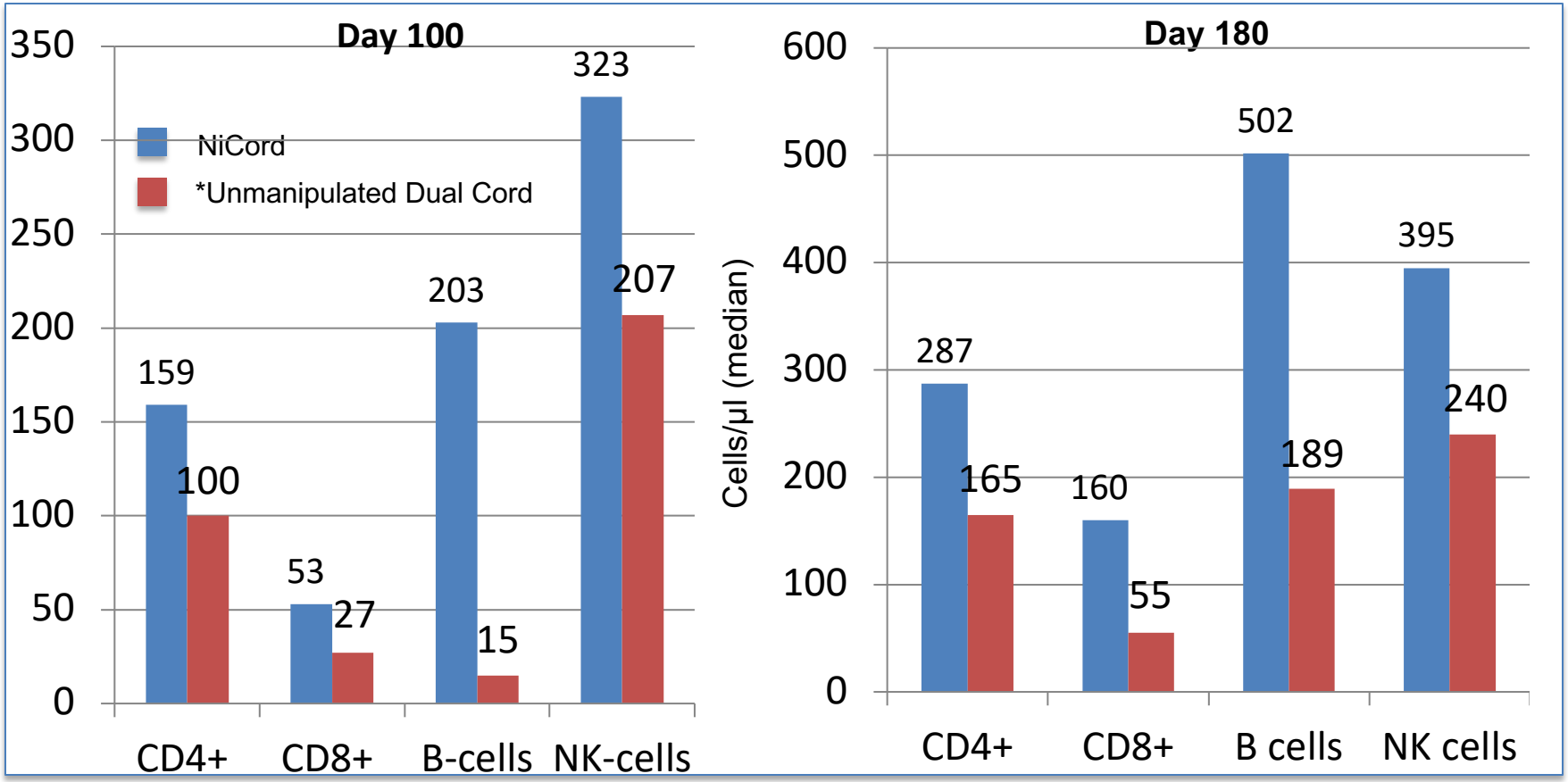


NiCord Phase I/II: Chronic Graft vs. Host Disease





Immune Reconstitution: NiCord vs. Unmanipulated Dual Cord



*Barker et al: Results of a prospective multicenter; myeloablative adult double-unit cord blood transplantation trial N=56 Brit J Haem 2015

NiCord Single Cord Phase I/II Study Results Summary; n=36

Endpoint	
Time to neutrophil engraftment (median)	11 days (range 6-26)
Time to platelet engraftment (median)	34 days (range 25-96)
aGvHD grade II-IV and III-IV at 100 days	44% and 11%
cGvHD Moderate-Severe at 1 year	10%
Graft Failure	Primary-1, Secondary-2 (HHV6-1, Adenovirus-1)
Chimerism (engrafted patients n=34)	Full donor (>95%); 97% Mixed chimerism; 3%
Transplant Related Mortality at 1 year	20%
Disease-free/Overall Survival at 1yr	49%/51%

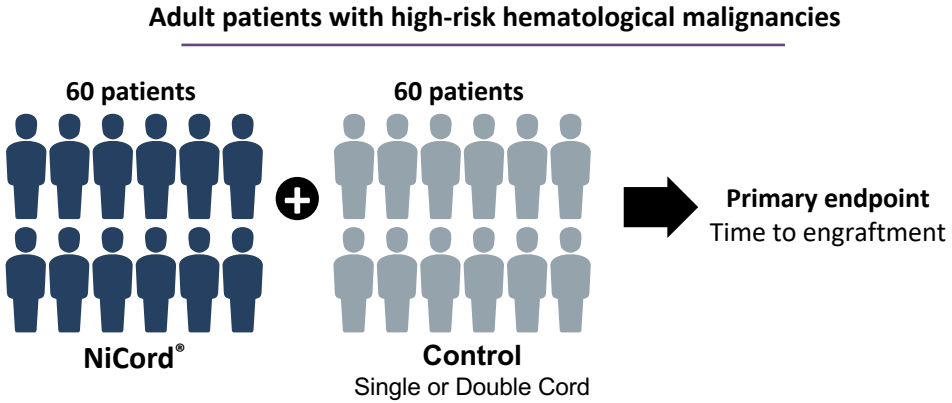
Median follow-up of survivors: 14 months (range 5-37)

Conclusions

- NiCord
  - Median 10 day reduction in time to neutrophil engraftment
  - Median 12 day reduction in time to platelet engraftment
    - Compared to standard myeloablative umbilical cord blood transplantation (CIBMTR)
  - Robust and durable engraftment > 7 years
  - Elimination of need for dual umbilical cord blood grafts
  - Reduced risk of bacterial infections
  - Fewer days in hospital during first 100 days post transplantation
    - Compared to single center matched historical control cohort
      - *Anand/Horwitz et al. BBMT 2017*

NiCord vs. Standard Umbilical Cord Blood Transplantation
Phase III Registration Trial (FDA and EMA)

- NiCord vs. Standard (single or double) UCBT
- Myeloablative conditioning
- Sponsor: Gamida Cell
- USA, Europe, Asia
- Open for accrual



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Steven Wease

Sheba Medical Center

Laurence Friedman

Co-Investigators

G. Sanz, P. Montesinos- Valencia
Pau Montesinos- Valencia
P. Stiff- Chicago
D. Valcarcel- Barcelona
M. Jagasia- Nashville
D. Cilloni- Turin
J. Boelens, J. Kuball- Utrecht
R. Hanna- Cleveland
L. Piu, W. Hwang- Singapore
J. Wagner, C. Brunstein- Minnesota

Patients and Families