



Transplantation of Ex vivo Expanded Umbilical Cord Blood (NiCord®) Results in Decreased Infection Burden and Hospital Length of Stay in the First 100 Days

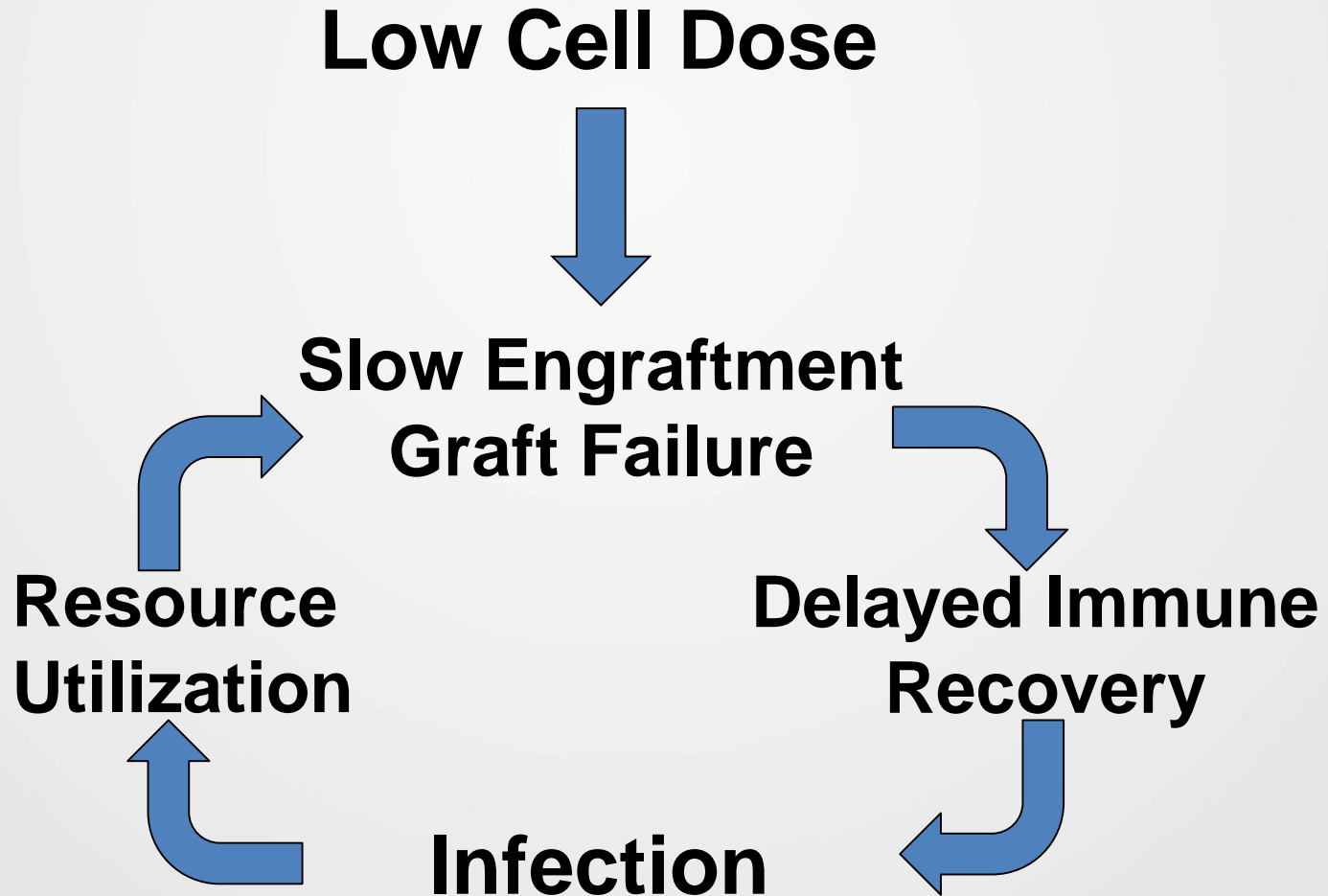
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DUKE CANCER INSTITUTE

A National Cancer Institute-designated Comprehensive Cancer Center

Limitations of adult umbilical cord blood (UCB) transplantation



NiCord[®] Graft Processing and Transplantation Schema

CD133+ Fraction



CD133- Fraction

II. NiCord[®] non-cultured Fraction (NF) → cryopreserved

I. NiCord[®] cultured fraction (CF)

Cultured with cytokines (FLT3, SCF, TPO, IL-6)

+ **Nicotinamide** (2.5mM) for 21± 2 days

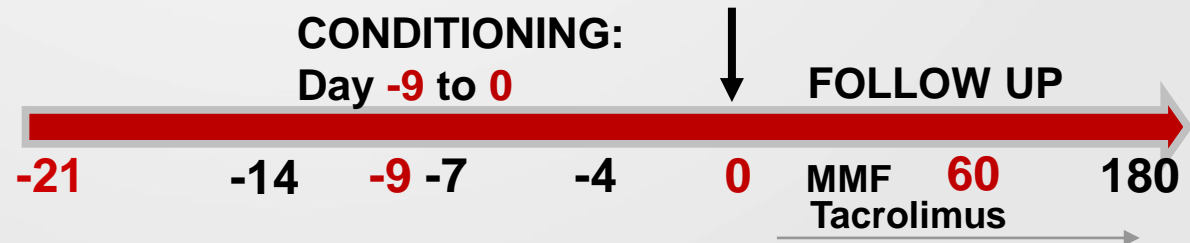
- Cells harvested, safety and quality tested
- Transported fresh or cryopreserved to transplant center

TRANSPLANTATION

I. NiCord[®] CF

II. NiCord[®] NF

III. +/-Unmanipulated CBU



NiCord Phase 1 Trial Outcomes

- NiCord cultured fraction expansion:
 - Median 486-fold (171-643) nucleated cell expansion
 - Median 72-fold (16-186) CD34+ cell expansion
 - Median CD34+ cell dose $3.5 \times 10^6/\text{kg}$ in Nicord vs. $0.07 \times 10^6/\text{kg}$ in unmanipulated unit
- Neutrophil recovery median 13 days
- Engraftment:
 - 8 patients with complete or partial myeloid and T cell engraftment from NiCord unit
 - 2 patients with engraftment from unmanipulated unit
 - 1 patient with engraftment failure

Study Rationale

- Question:
 - Is rapid hematopoietic recovery after NiCord transplantation associated with clinical benefit in the early post-transplantation period compared to a historical control of standard UCB patients?
- Endpoints:
 - Infectious complications in the first 100 days
 - Length of hospital stay in the first 100 days

Methods

- Study population:
 - Cohort 1: 18 consecutive adult recipients of NiCord grafts from January 2010-March 2015
 - Cohort 2: 88 consecutive adult recipients of standard single or double UCB grafts January 2005-March 2015
- Infection episodes
 - categorized by type and severity
 - BMTCTN Technical MOP version 3.0
 - mean number of infections per 100 patient days
 - Accounts for multiple infections per patient
- Length of hospitalization
 - Days alive and out of the hospital in the first 100 days
 - Account for early deaths (Ballen et al *BBMT* 2015)

Baseline patient characteristics

	Nicord (N=18)	Standard UCB (N=88)	P
	N (%)	N (%)	
Age – Median (IQR)	45 (42 - 56)	38 (28 - 51)	0.035
Pre-Transplant Weight – Median (IQR)	91.15 (76 - 98.1)	77.78 (65.4 - 91.4)	NS
Male Sex	9 (50%)	47 (53.4%)	NS
CMV +	13 (72.2%)	49 (55.7%)	NS
KPS – Median (IQR)	90 (80 - 90)	90 (80 - 90)	NS
Transplant Diagnosis			NS
Acute Leukemia/MDS	16 (88.9%)	78 (88.6%)	
Lymphoid Malignancy	2 (11.1%)	10 (11.4%)	
Disease Status ¹			NS
Early	8 (44.4%)	30 (34.1%)	
Non-Early	10 (55.6%)	58 (65.9%)	

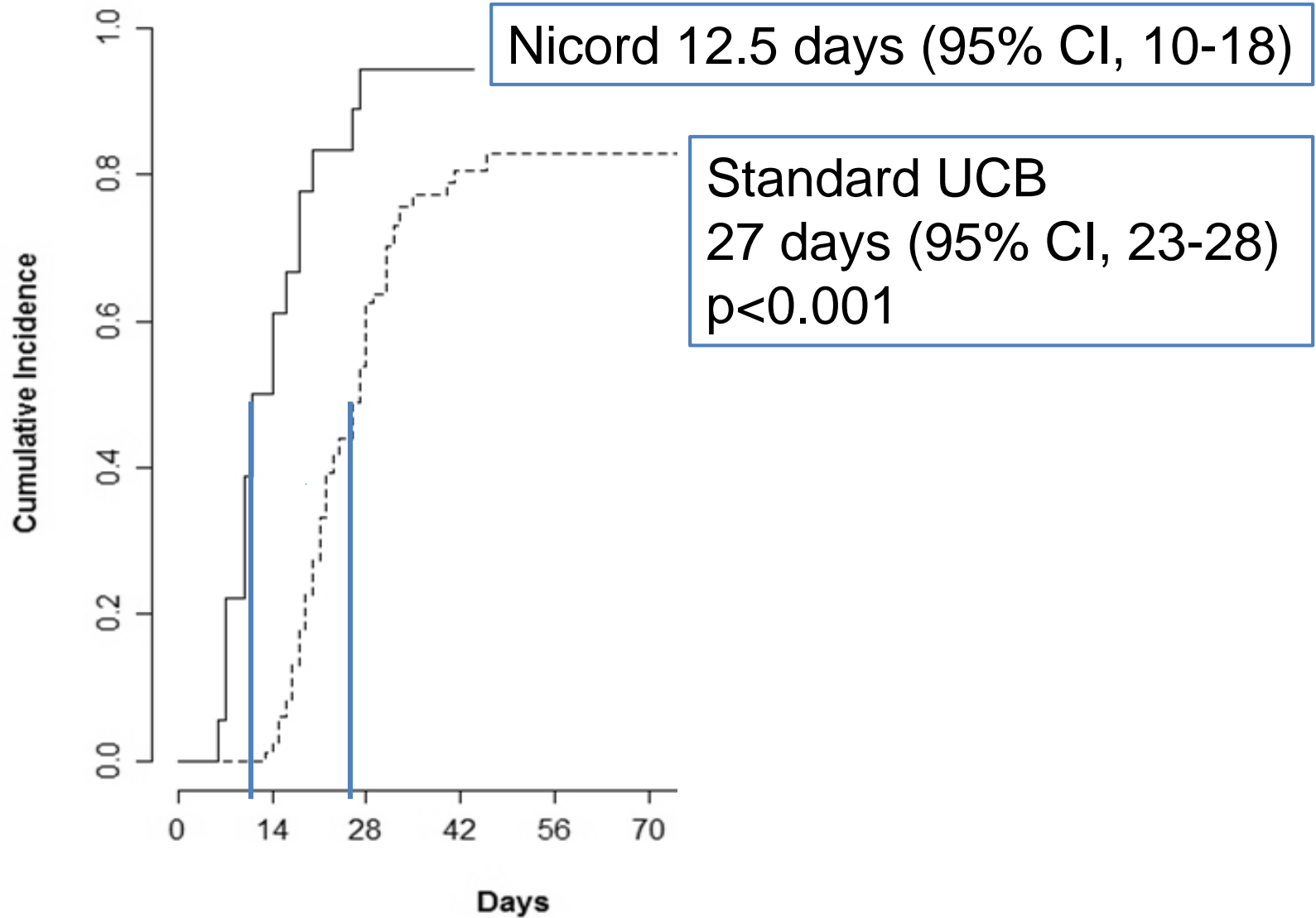
¹ Early defined as acute leukemia transplanted in first complete remission (CR), MDS transplanted untreated or in first CR, CML in first chronic phase, and NHL and MM transplanted either untreated or in first CR per EBMT risk score

Baseline transplant characteristics

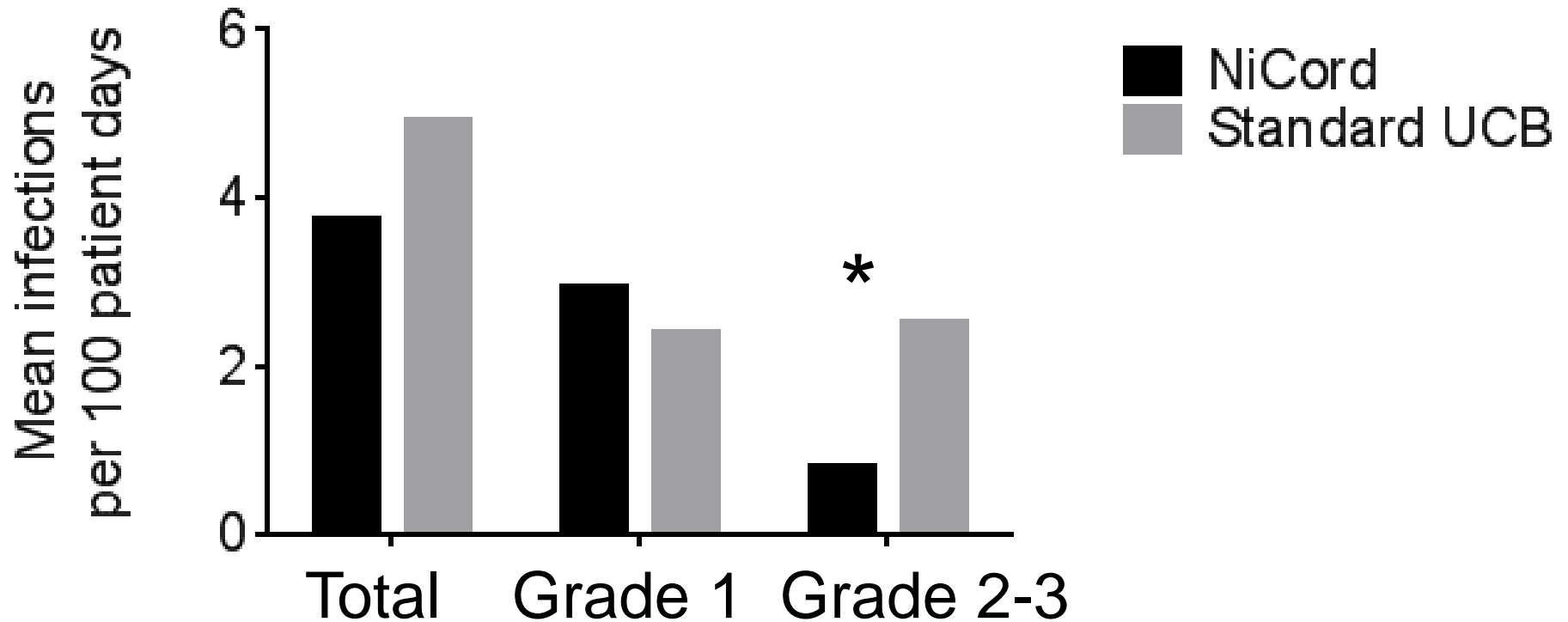
	Nicord (N=18)	Standard UCB (N=88)
	N (%)	N (%)
UCB Type		
Single UCB	7 (38.9%)	4 (4.5%)
Double UCB	11 (61.1%)	84 (95.5%)
HLA Match		
4/6	6 (33.3%)	4 (4.5%)
5/6	1 (5.6%)	0 (0%)
4/6 + 4/6	5 (5.6%)	45 (51.1%)
4/6 + 5/6	3 (16.7%)	18 (20.5%)
4/6 + 6/6	0 (0%)	2 (2.3%)
5/6 + 5/6	1 (5.6%)	11 (12.5%)
5/6 + 6/6	2 (11.1%)	3 (3.4%)
6/6 + 6/6	0 (0%)	5 (5.7%)
Conditioning		
1,350 cGy TBI/fludarabine	11 (61.1%)	47 (53.4%)
1,350 cGyTBI/fludarabine/cyclophosphamide	7 (38.9%)	17 (19.3%)
1,350 cGy TBI/fludarabine/thiotepa ¹	0 (0%)	24 (27.3%)

¹One patient received 200 cGy TBI/fludarabine/cyclophosphamide/thiotepa

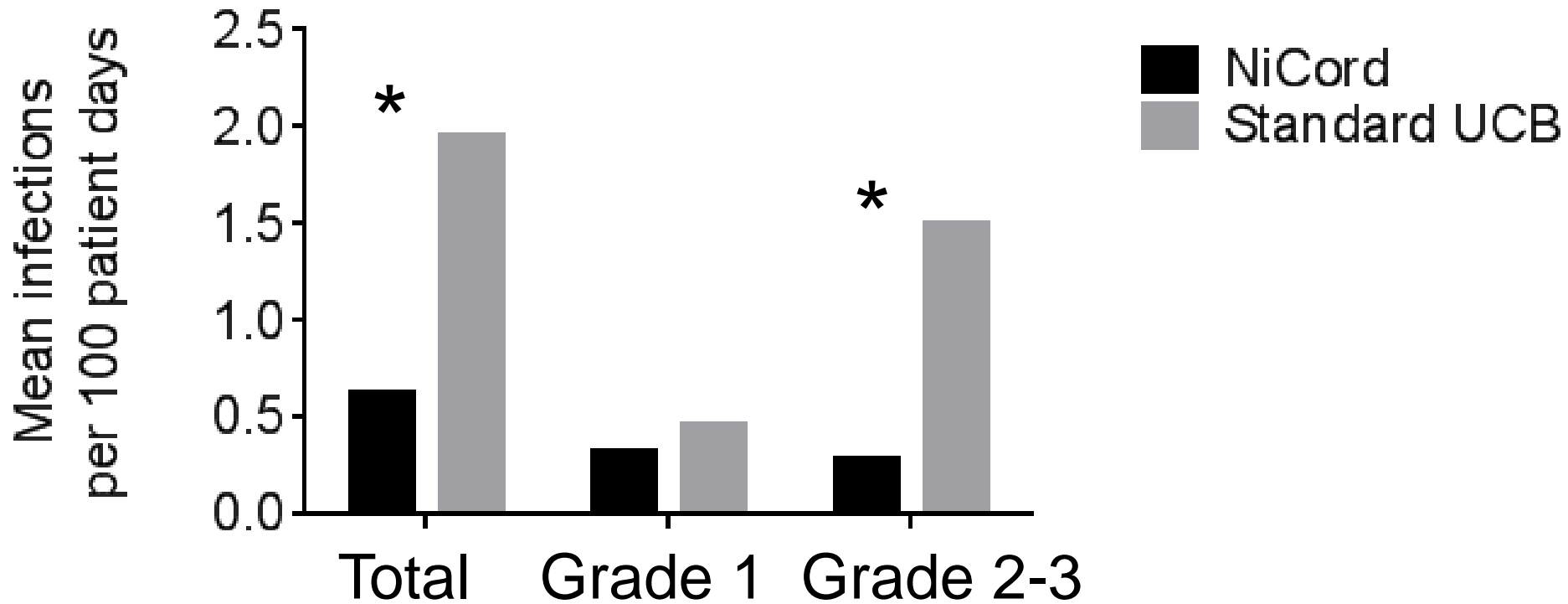
Median days to neutrophil recovery



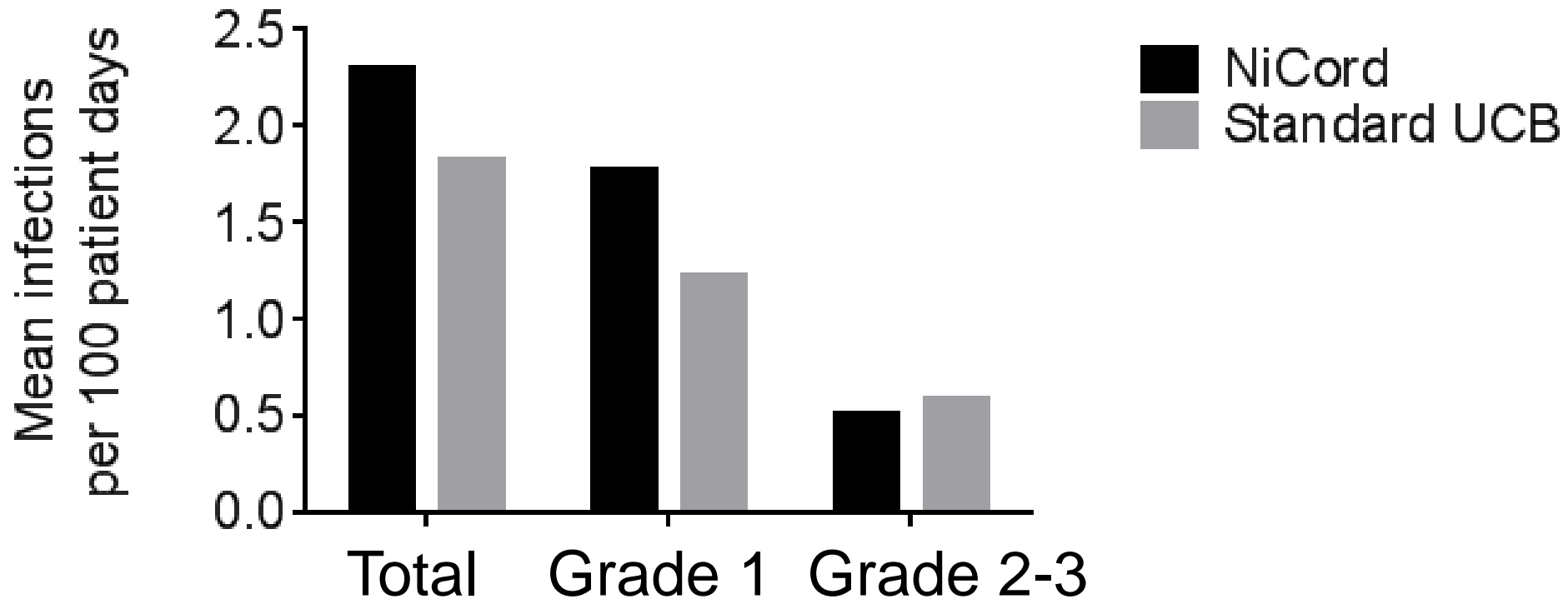
Total infections per patient in first 100 days post-transplantation



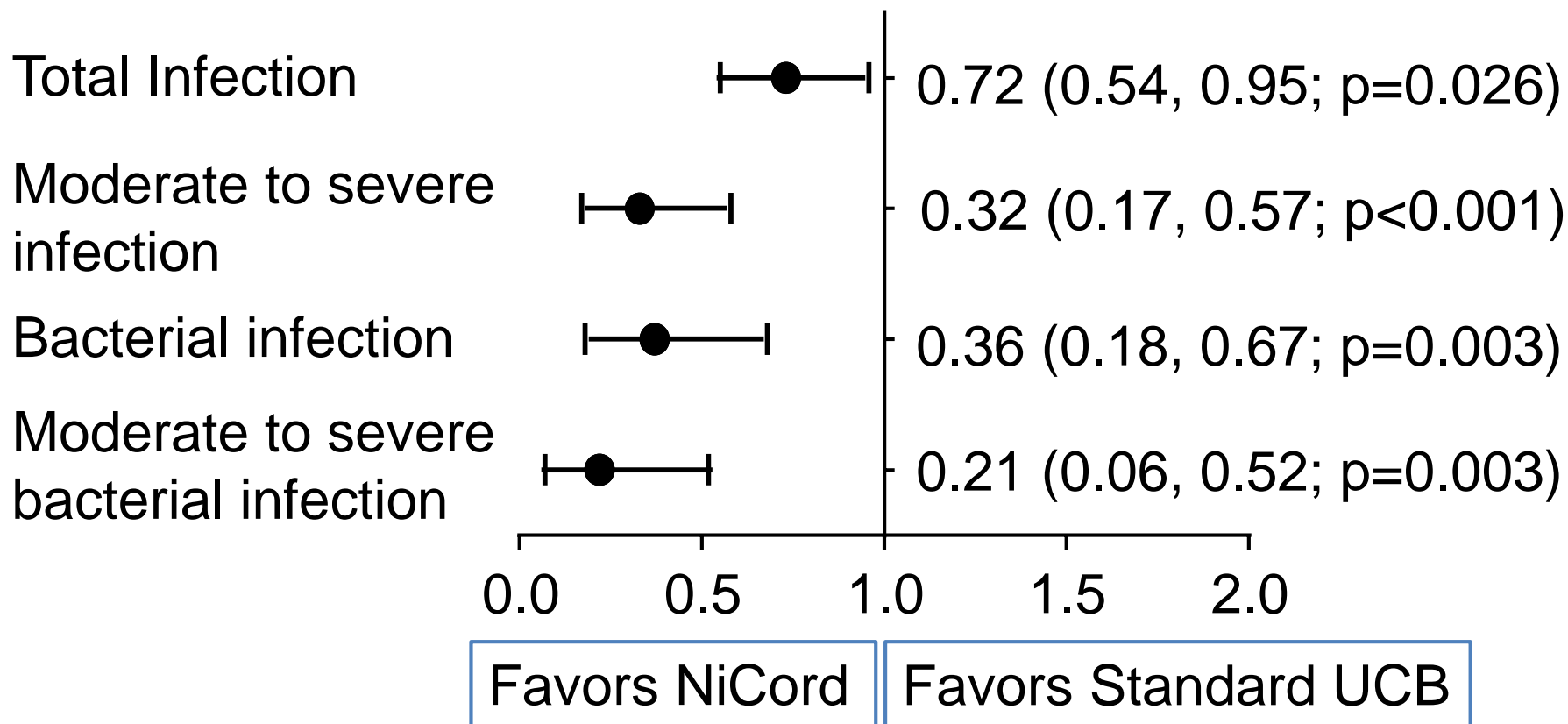
Bacterial infections per patient in first 100 days post-transplantation



Viral infections per patient in first 100 days post-transplantation

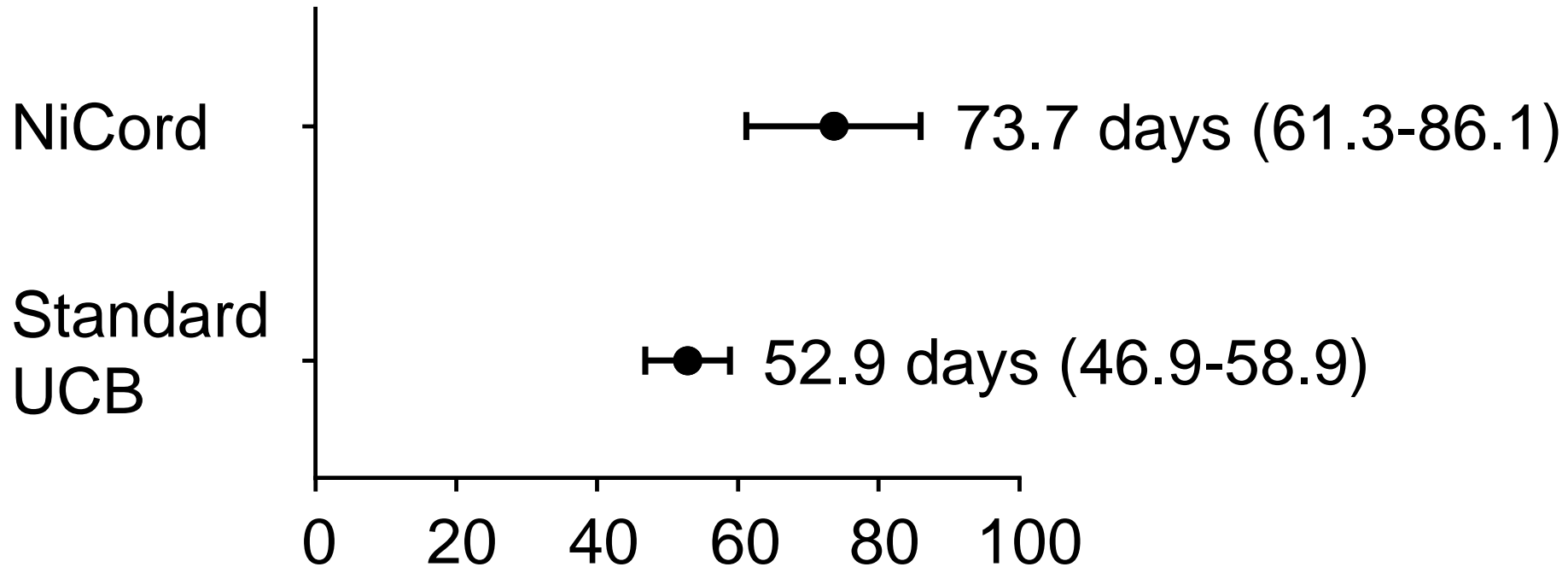


Adjusted relative infection density



Relative risk of infection adjusted for age, disease status, and severe acute GVHD by Poisson regression (95% CI; p)

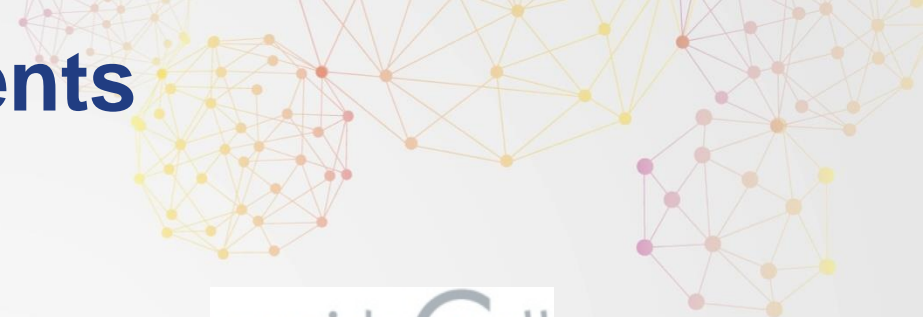
Days alive and out of the hospital in first 100 days post-transplantation



Mean days alive and out of the hospital
adjusted for age, KPS, and severe acute
GVHD by ANCOVA (95% CI; $p=0.002$)

Summary

- Transplantation of NiCord expanded umbilical cord blood stem cells provides early clinical benefit:
 - Rapid neutrophil engraftment
 - Reduced total and bacterial infection burden
 - Decreased hospital length of stay
- These data provide justification for a prospective, randomized phase III study of NiCord versus Conventional umbilical cord blood transplantation
 - To open in EU and US in mid 2016



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