Improved Clinical Outcomes with Omidubicel versus Standard Myeloablative Umbilical Cord Blood Transplantation: Results of a Phase III Randomized, Multicenter Study

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Disclosures

- Gamida Cell- institutional research funding

- Magenta- advisory board participation

- Kadmon- advisory board participation

- CareDx- advisory board participation

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 transplant-related morbidity and mortality
  - Increased resource utilization

Potential Solution

Ex-vivo Expansion Cord Blood Stem Cells

Nicotinamide Alters Metabolic Pathways Mimicking Bone Marrow Endosteum

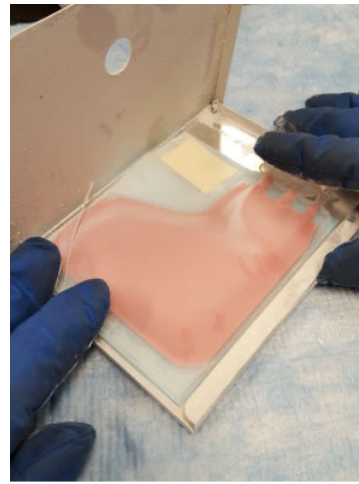

CD133- Fraction

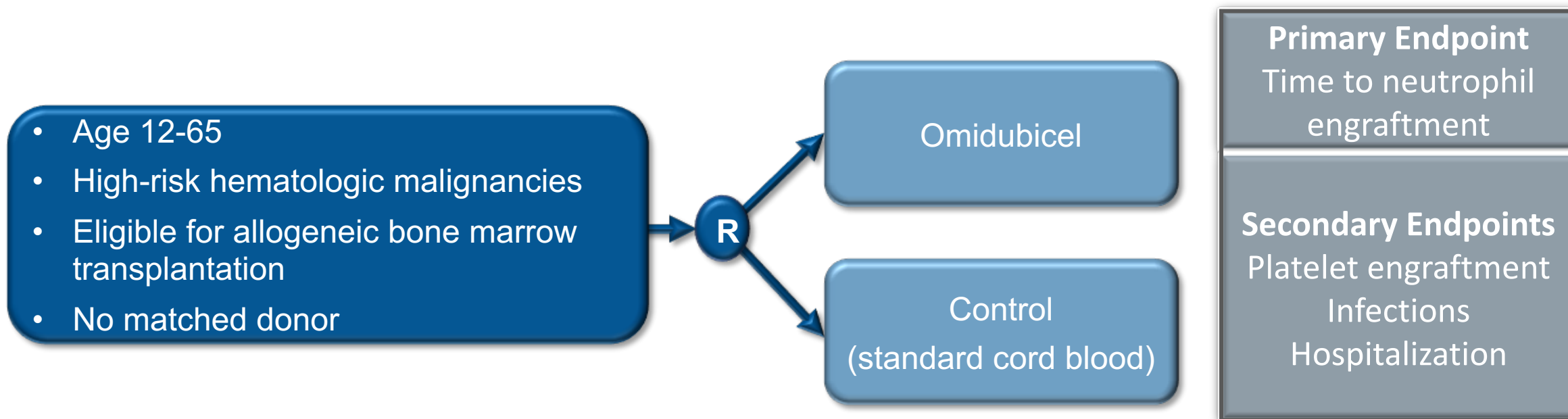**CD133+ Fraction**
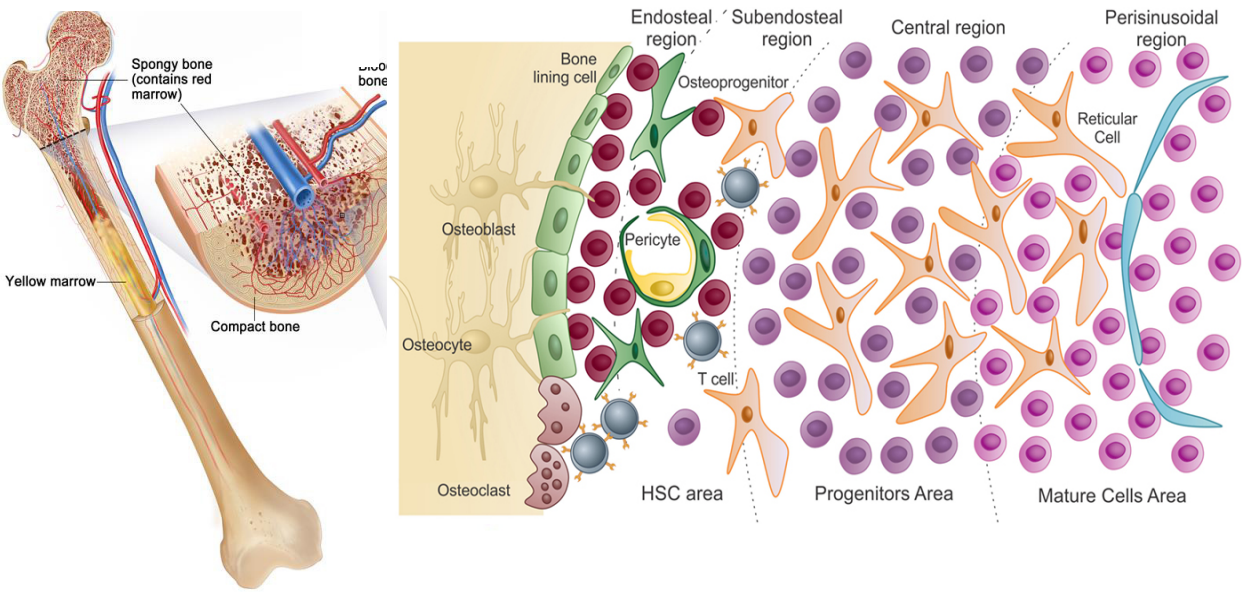
Importance of Nicotinamide

- Plays a key role in metabolic reprogramming of cells

- Is a master regulator of NAD-related signaling pathways

- Directly involved in control of redox-sensitive enzymes

- Preserves cellular functionality and phenotype during expansion

Phase 3 Registration Study of Omidubicel

Inclusion criteria:
- Age 12-65
- High-risk hematologic malignancies
- Eligible for allogeneic bone marrow transplantation
- No matched donor

R (Randomization)

→ Omidubicel

→ Control (standard cord blood)

Primary Endpoint
Time to neutrophil engraftment

Secondary Endpoints
Platelet engraftment
Infections
Hospitalization

- Cord blood units selected prior to randomization
- Randomization stratified by:
  - Treatment center
  - Disease risk index
  - Age
  - Intent to perform single vs double cord transplant in the control arm
- Minimization algorithm was used to balance prognostic factors in the treatment groups.

Enrollment Completed: 12/2019
Day 180 Follow Up Completed: 9/2020

Patient Disposition
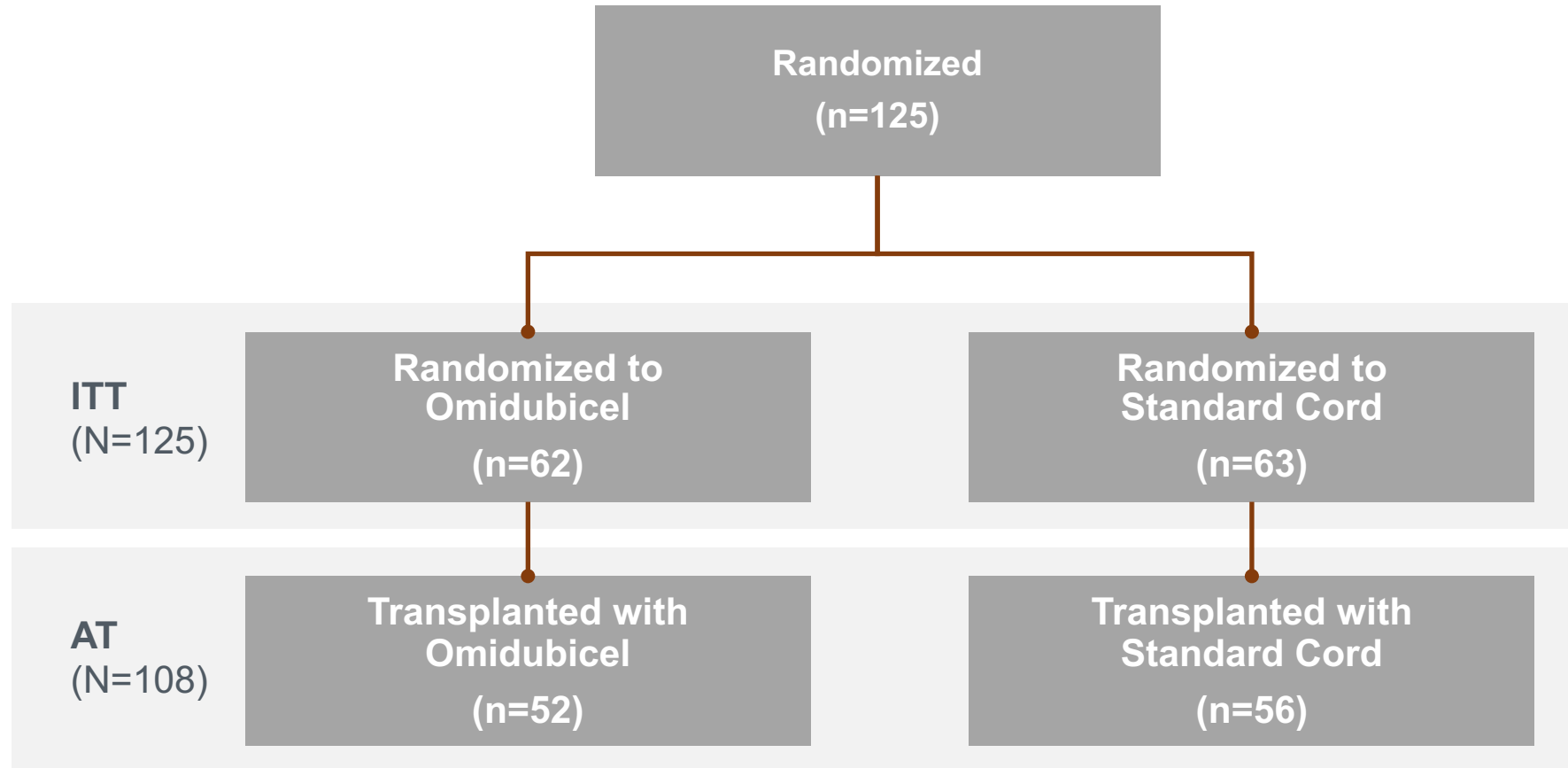
ITT: Intent to Treat; AT: As Treated population: received transplantation with omidubicel or standard cord per protocol.

Demographics | Intent-to-Treat (ITT) Population

		Omidubicel (N=62)	Control (N=63)
Gender	Female	30 (48%)	23 (37%)
	Male	32 (52%)	40 (63%)
Age (y)	Median (range)	40 (13-62)	43 (13-65)
	12-17	8 (13%)	6 (10%)
	18-39	23 (37%)	23 (36%)
	40-59	27 (44%)	31 (49%)
	60-65	4 (7%)	3 (5%)
Weight	Median (range)	78.6 (43-134)	77.4 (46-133)
Race	White	35 (57%)	37 (59%)
	Black	11 (18%)	9 (14%)
	Asian	7 (11%)	10 (16%)
	Other/Unknown	9 (15%)	7 (11%)
Ethnicity	Latino	10 (16%)	6 (10%)

Patient and Transplant Characteristics

		Omidubicel (N=62)	Control (N=63)
Disease	AML	27 (44%)	33 (52%)
	ALL	20 (32%)	21 (33%)
	MDS	6 (10%)	3 (5%)
	CML	4 (7%)	2 (3%)
	Lymphoma	3 (5%)	2 (3%)
	Rare Leukemia	2 (3%)	2 (3%)
Myeloablative Conditioning Regimen	TBI 1350cGy, Fludarabine, Thiotepa	7(11%)	9(14%)
	TBI 1320cGy, Fludarabine, Cyclophosphamide	24(39%)	21(33%)
	Thiotepa, Busulfan, Fludarabine	27(44%)	28(44%)
	Transplanted off-study	4(6%)	5(8%)
HLA match (CBU #1)	4/6	46 (74%)	46 (73%)
	5/6	15 (24%)	16 (25%)
	6/6	1 (2%)	1 (2%)
Intended CBU transplant	Single	20 (32%)	21 (33%)
	Double	42 (68%)	42 (67%)

Graft Characteristics
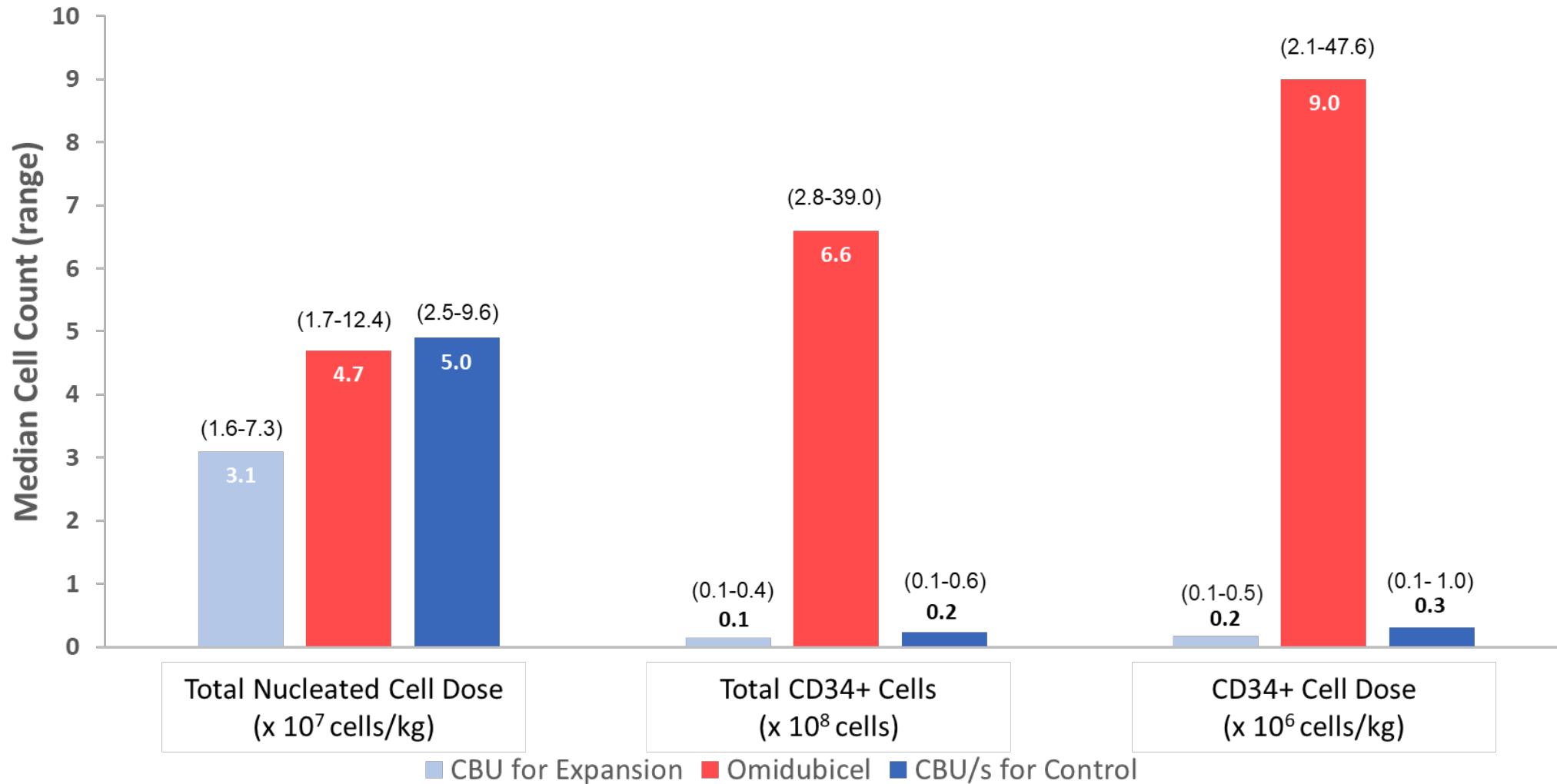
Primary Endpoint
Time to Neutrophil Engraftment (ITT)

Intent-to-treat	Median Time to Neutrophil Engraftment (Days)*	95% CI	
Omidubicel (N = 62)	12.0	(10.0, 15.0)	p<0.001**
Control (N = 63)	22.0	(19.0, 25.0)	

*Patients not transplanted or who do not engraft on/before Day 42 post transplant were assigned to Day 43
**Mann-Whitney test

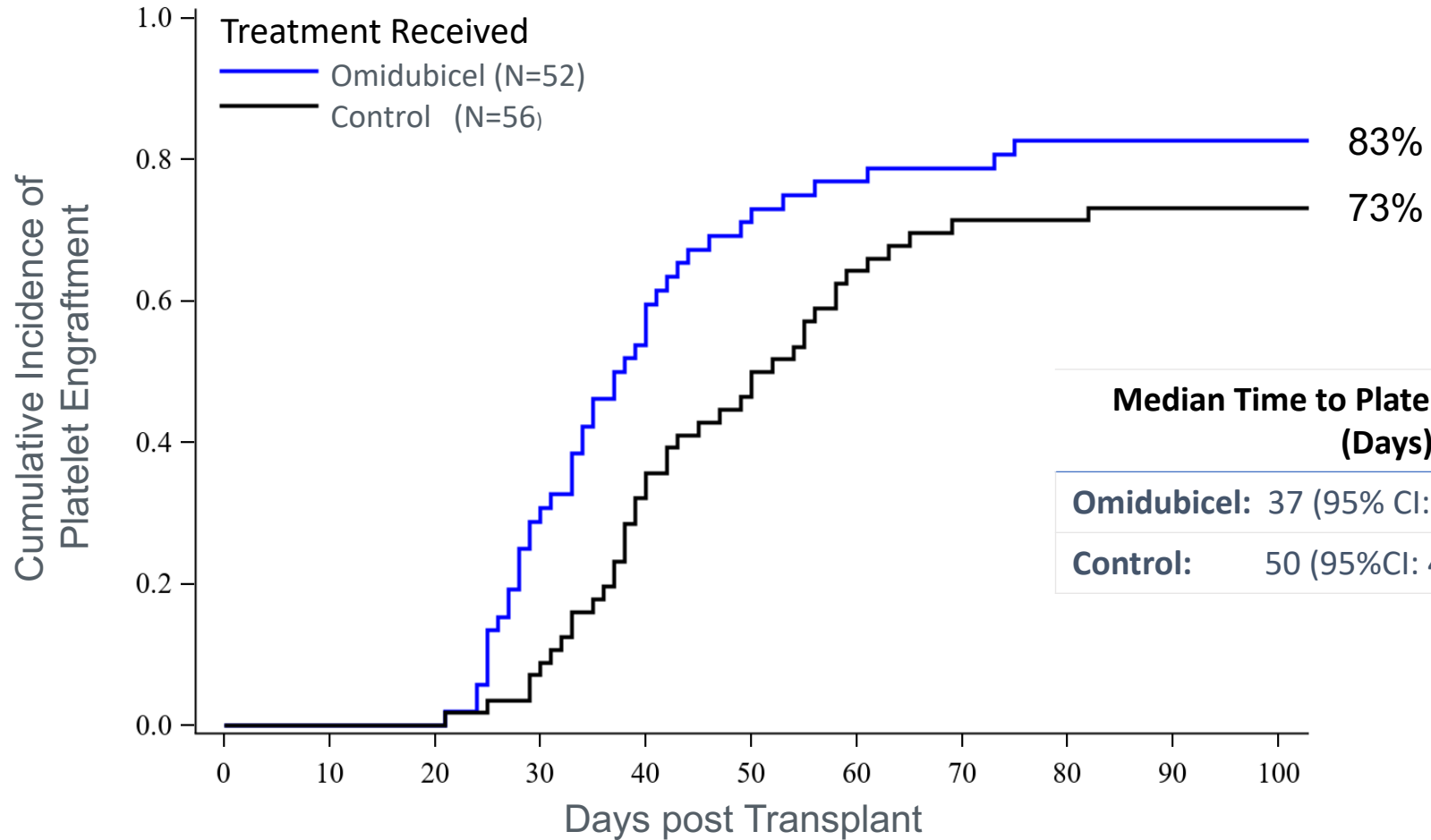# Day 42 Neutrophil Engraftment
(As-Treated Population N=108)

Secondary Endpoint: Platelet Engraftment by Day 42 (ITT Population)

| Intent-to-treat	Day 42 Cumulative Incidence	Difference in Cumulative Incidence	95% CI	P-Value
Omidubicel (N = 62)	0.55	0.20	(0.03, 0.35)	0.028
Control(N = 63)	0.35			

Day 100 Platelet Engraftment
As-treated population

Cumulative Incidence of Platelet Engraftment

Treatment Received
— Omidubicel (N=52)
— Control (N=56)

83%
73%

Median Time to Platelet Engraftment (Days)		P value
Omidubicel: 37 (95% CI: 33, 42)		p<0.023
Control: 50 (95%CI: 42, 58)		

Days post Transplant

N at risk

NiCord	52	52	52	36	22	12	7	5	3	3	2
UCB	56	56	56	51	35	23	11	7	7	6	4

Secondary Endpoint: Grade 2-3 Bacterial or Invasive Fungal Infection by 100 Days (ITT Population)
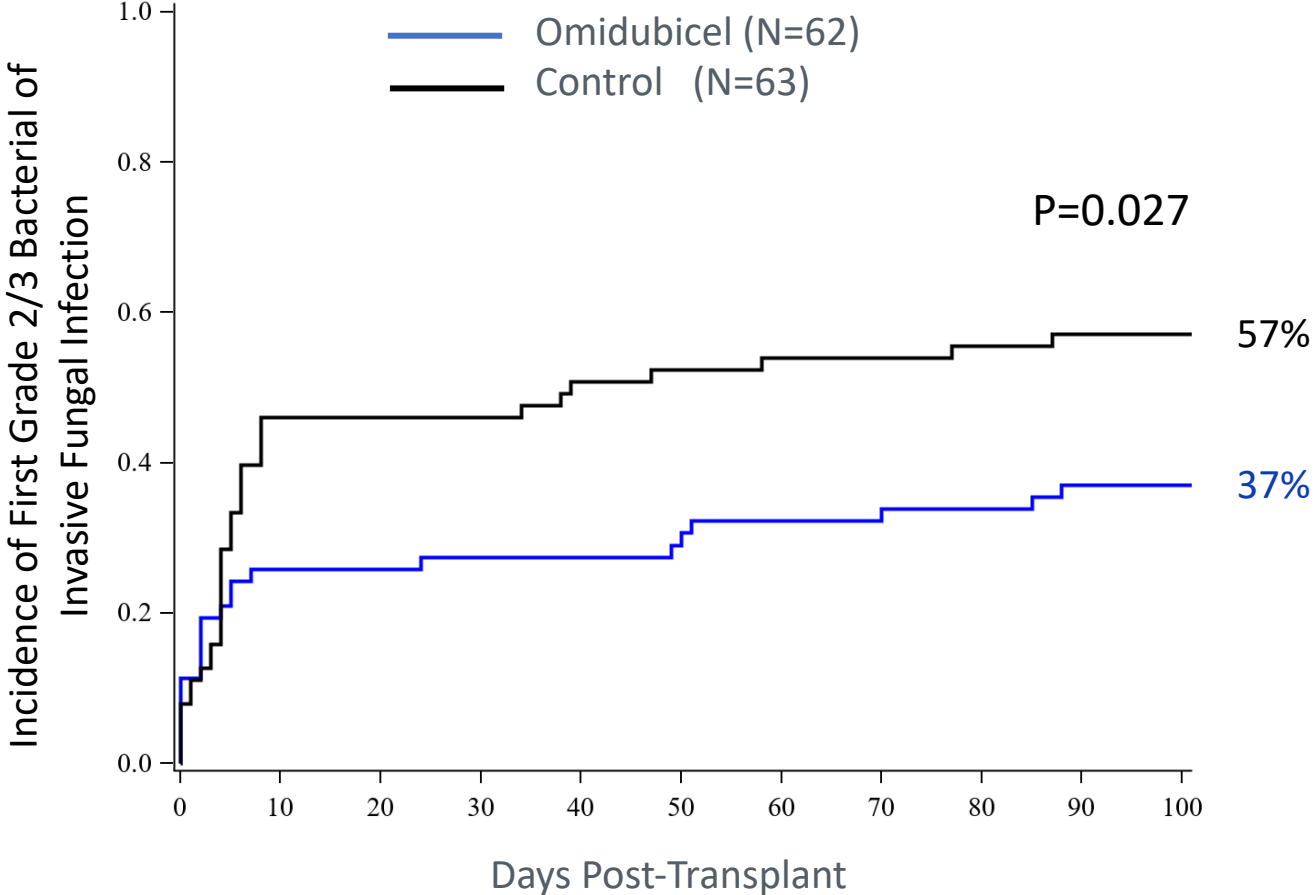
Fewer Viral Infections in Recipients of Omidubicel
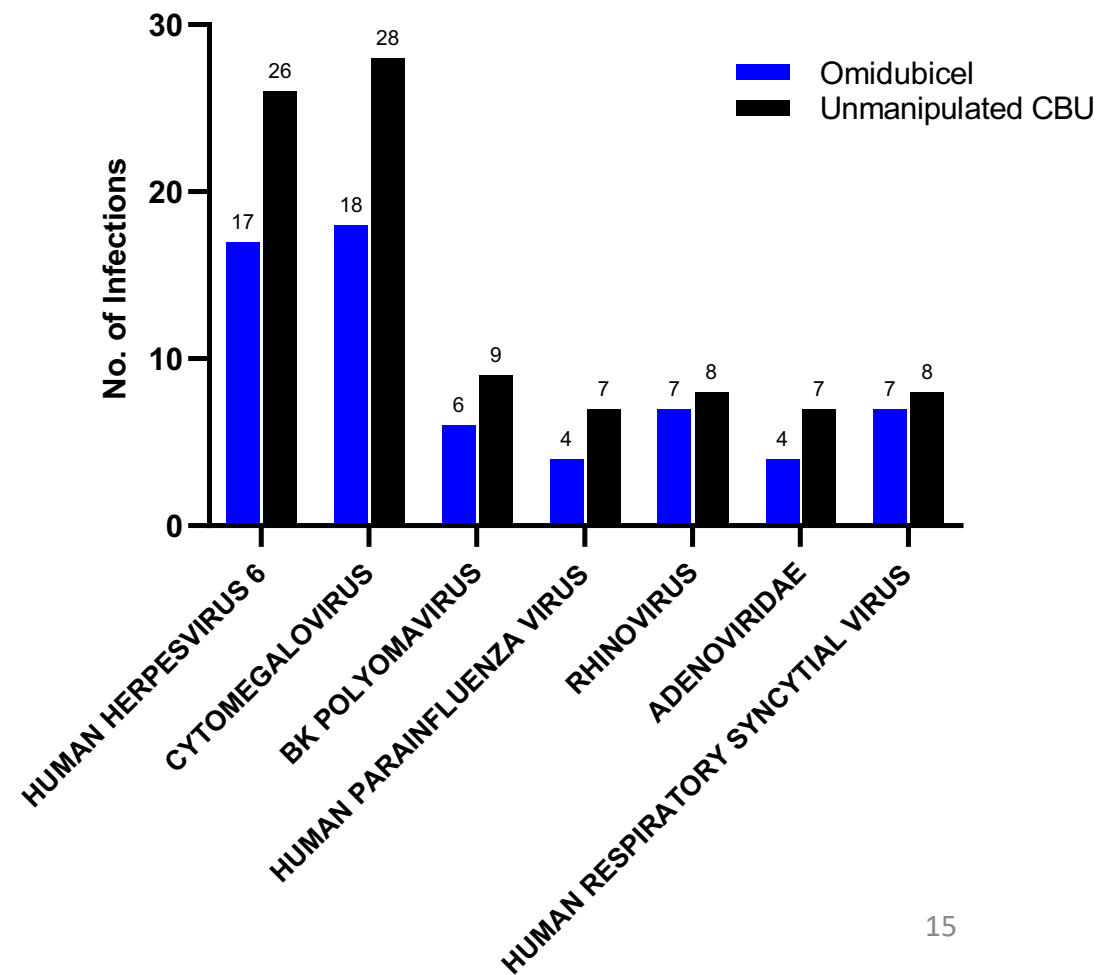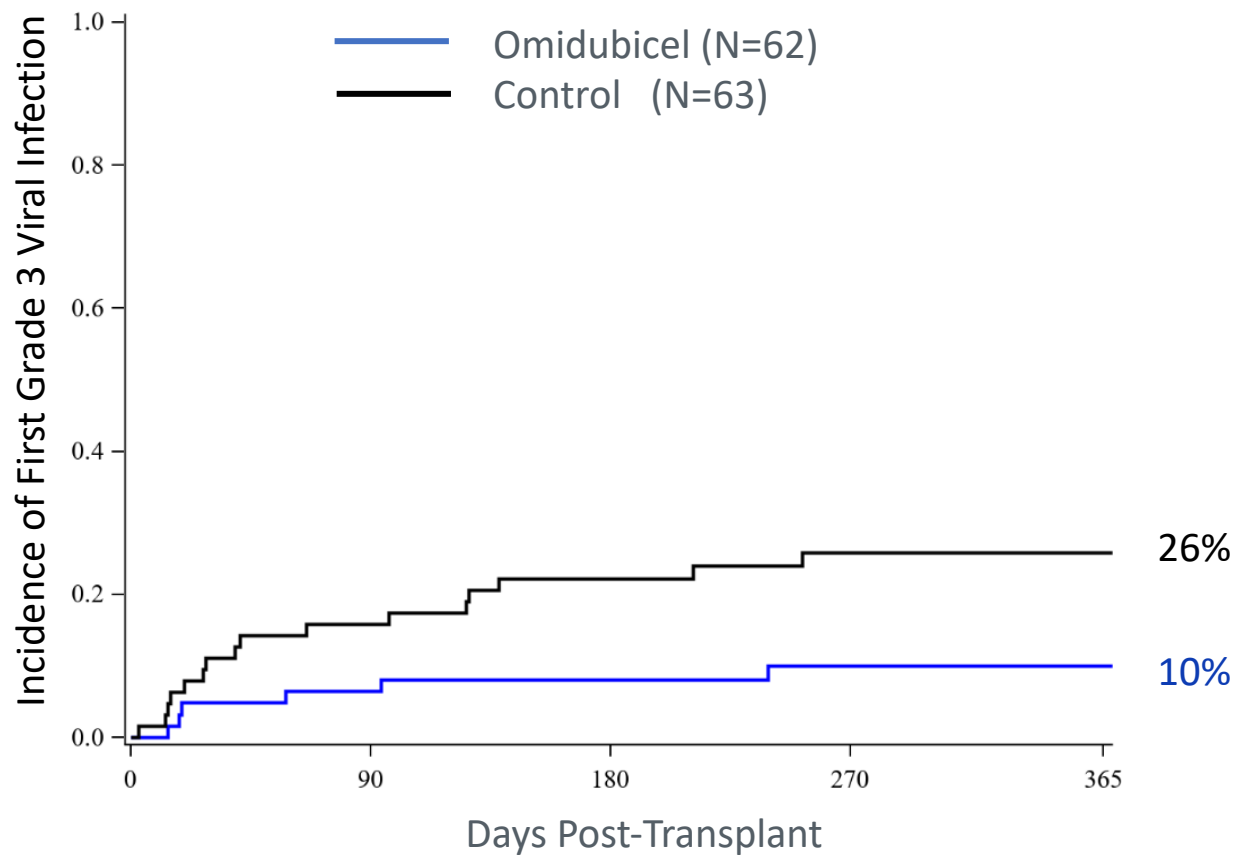
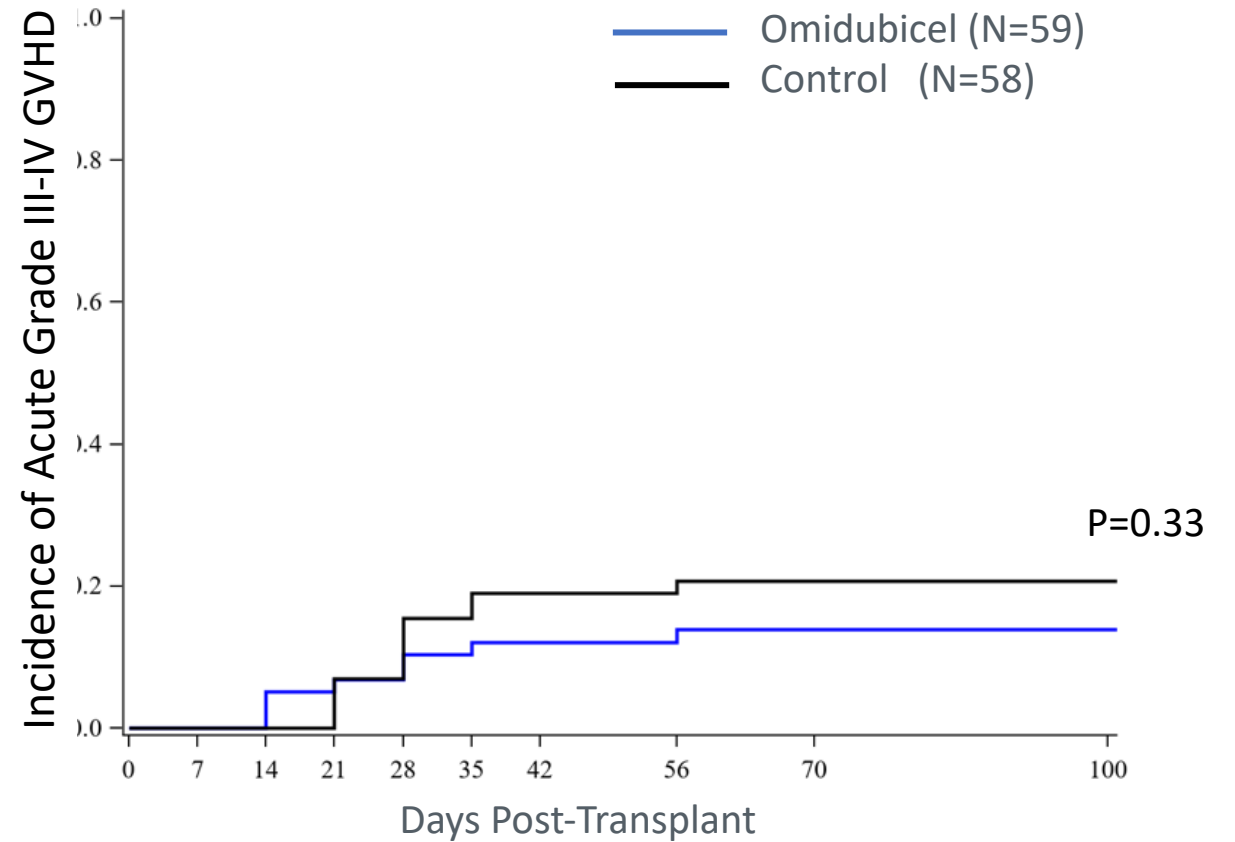# Secondary Endpoint: Days Alive and Out of the Hospital in the First 100 Days Post-Transplant (ITT Population)
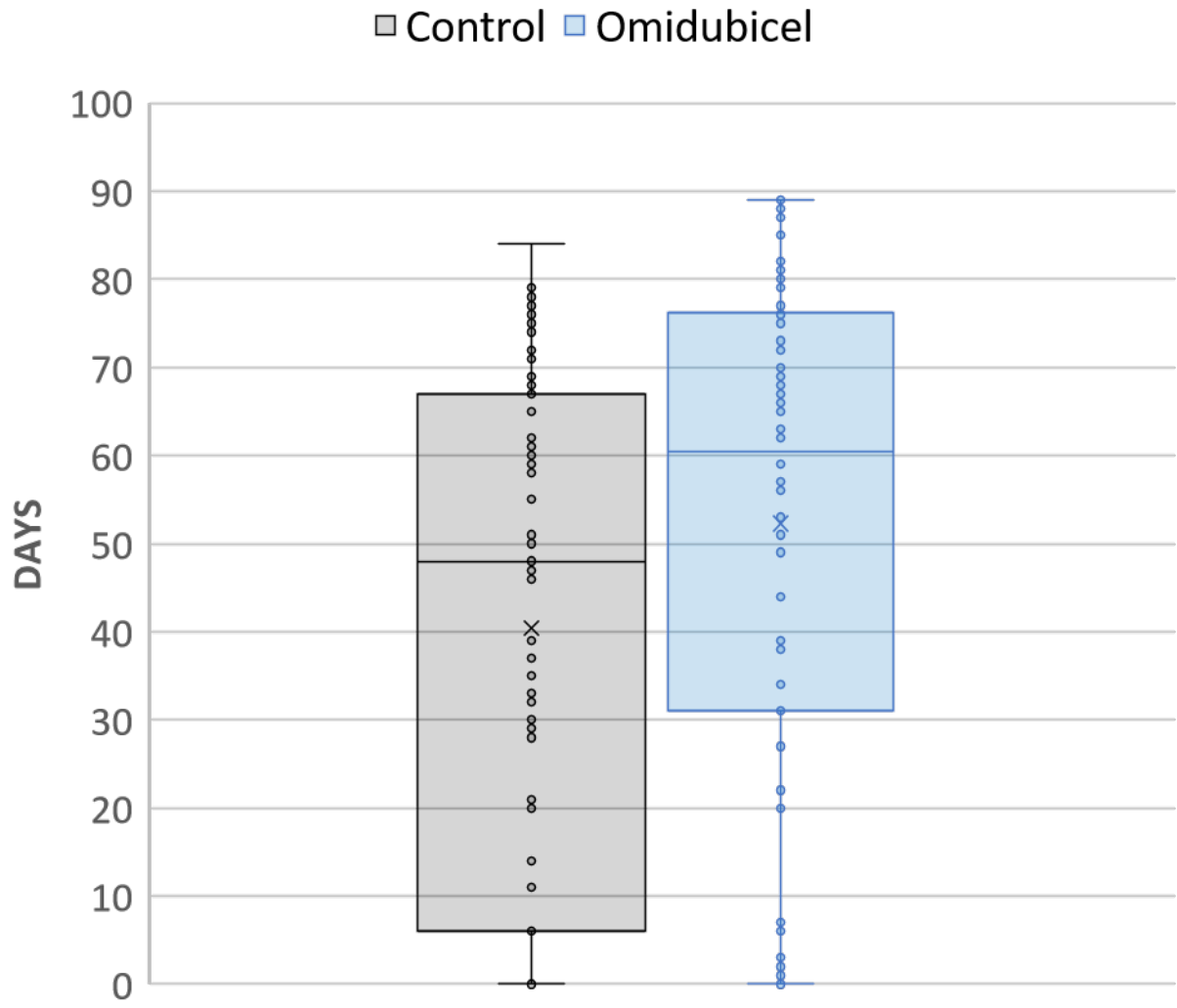
Omidubicel: Median 60.5 days
Control: Median 48.0 days
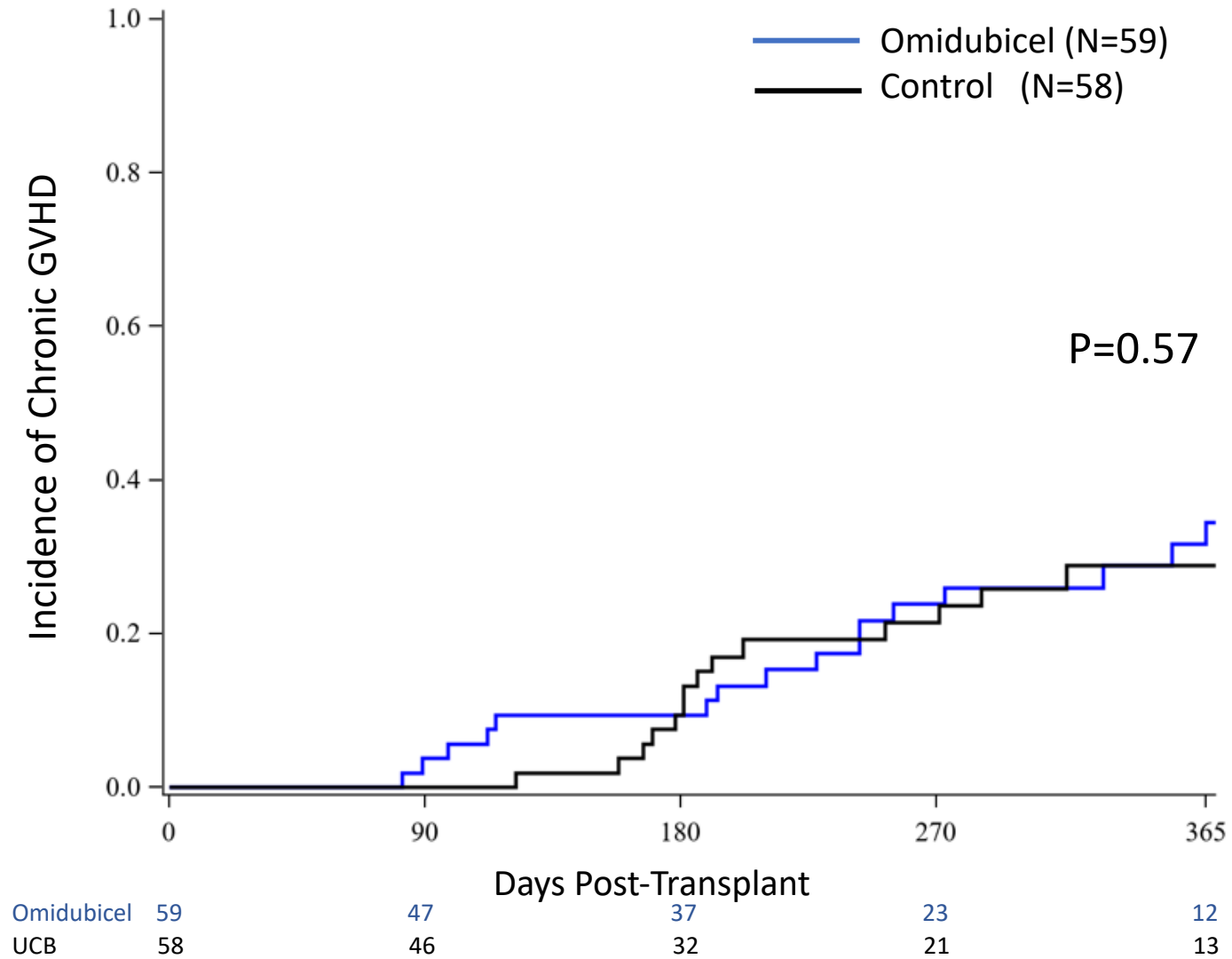p = 0.005

Acute GvHD

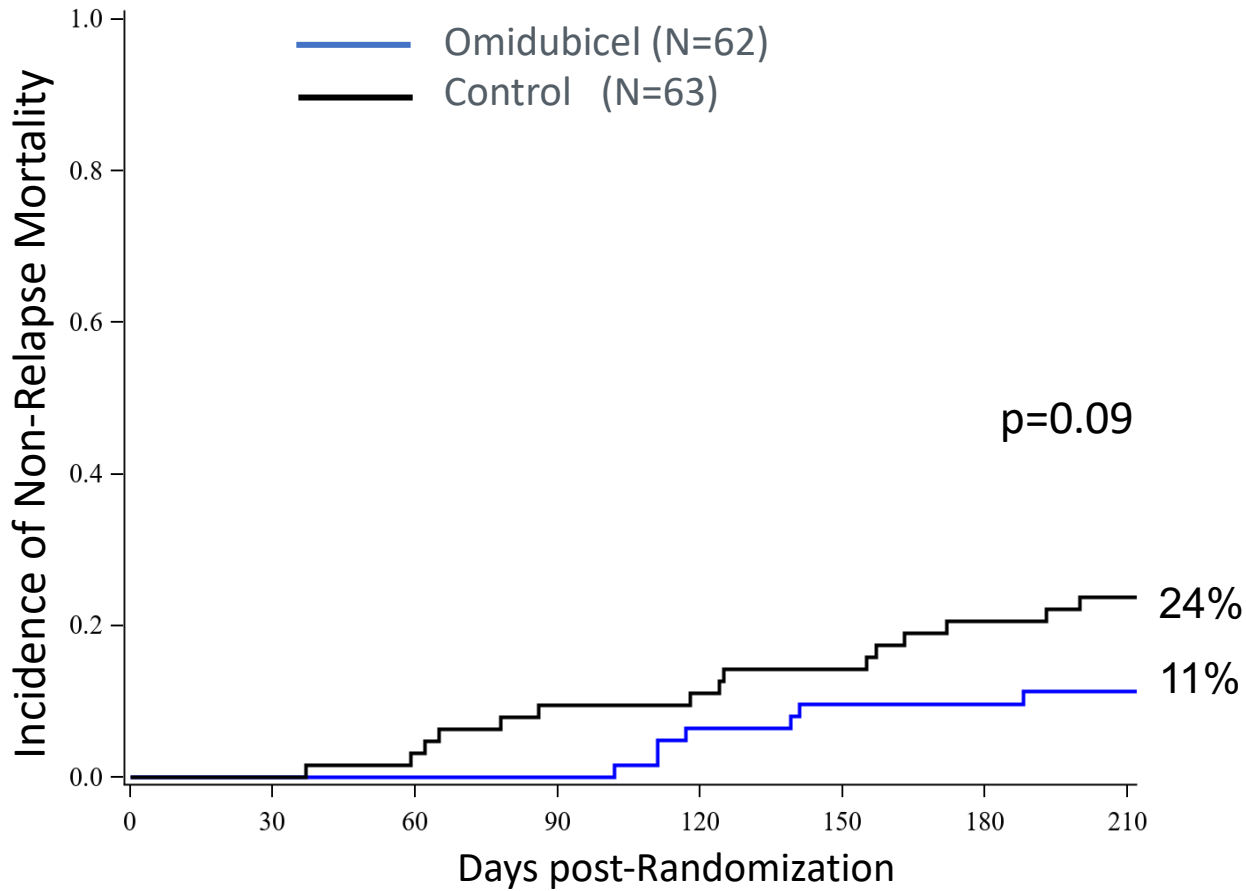Grade II-IV Acute GVHD Day 100
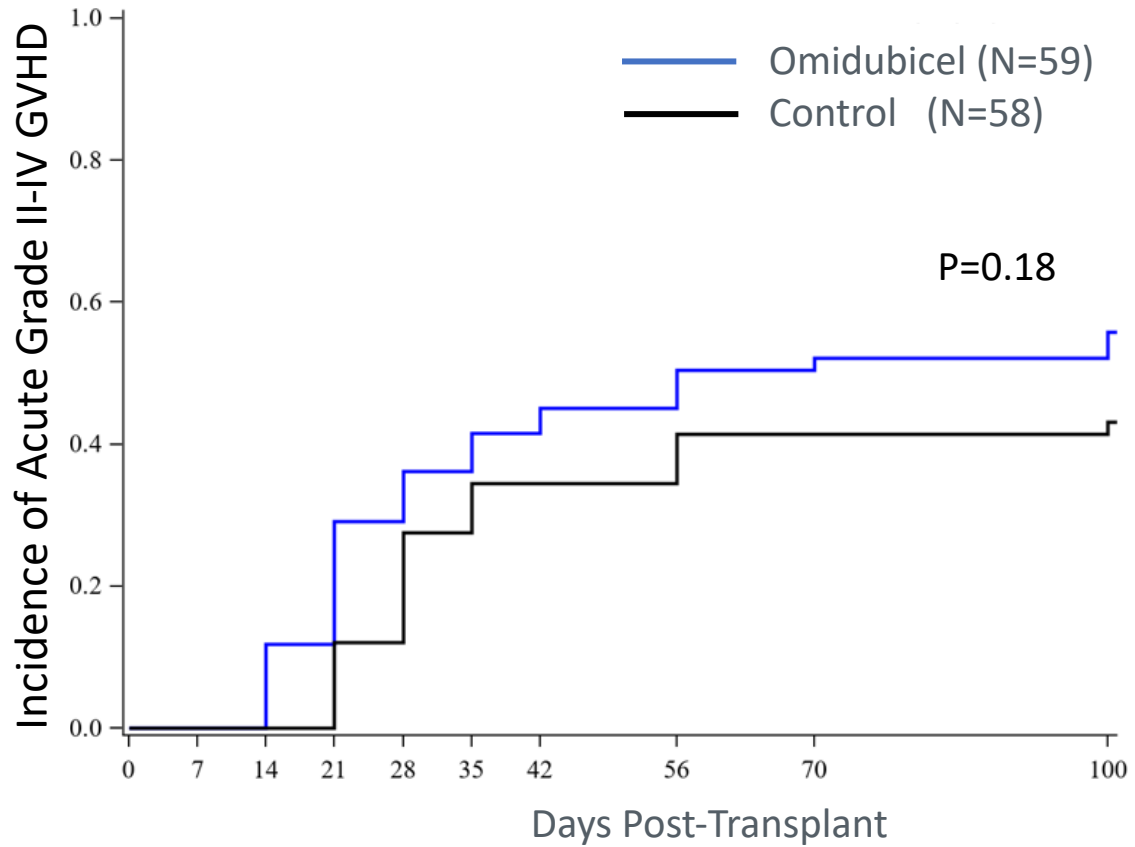
Grade III-IV Acute GVHD Day 100
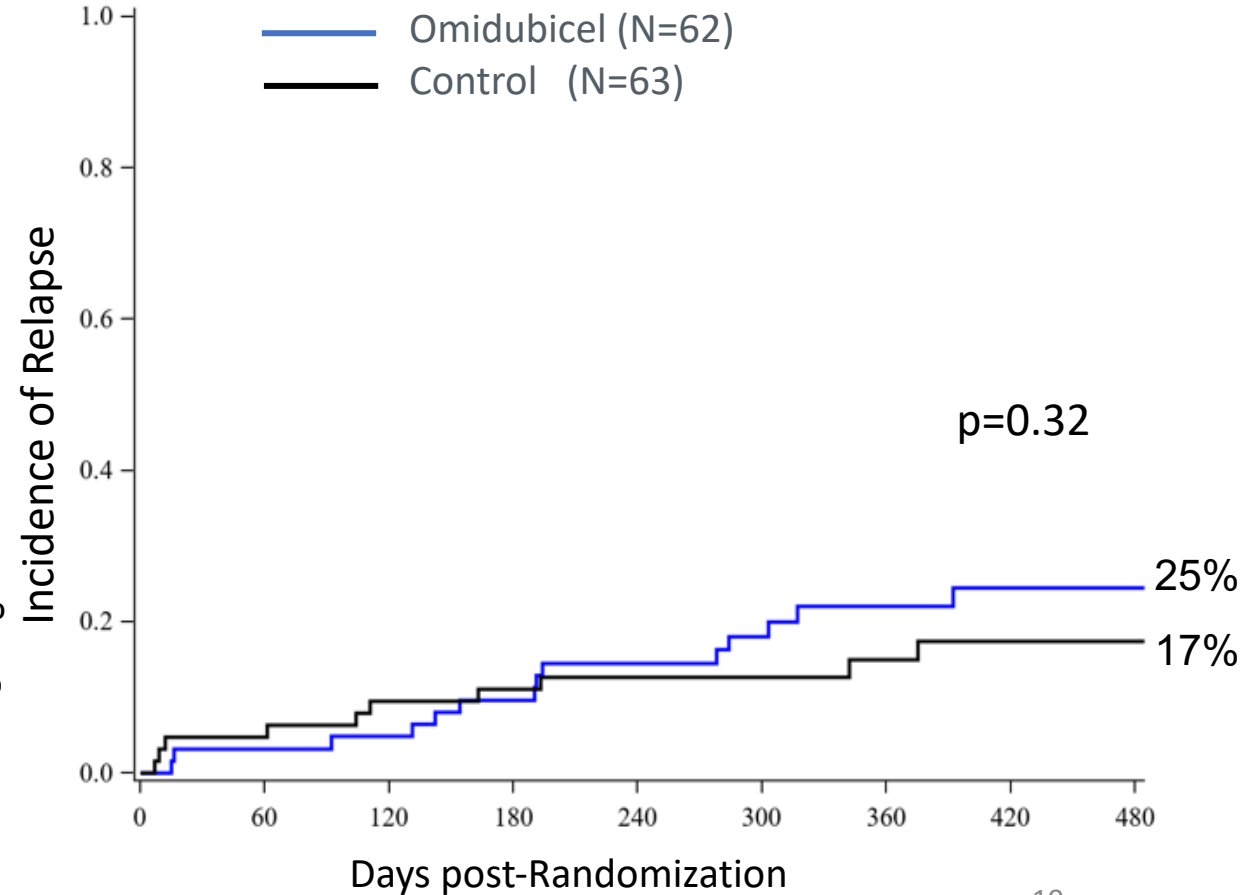
Chronic GvHD

All Grades Chronic GVHD 1 Year

Omidubicel (N=59)
Control (N=58)

P=0.57

Incidence of Chronic GVHD

Days Post-Transplant

Omidubicel 59	47	37	23	12
UCB 58	46	32	21	13

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Non-relapse Mortality and Relapse
(ITT Population)

Non-relapse Mortality

Relapse

Disease-free and Overall Survival
(ITT population)

Disease-free Survival — Overall Survival
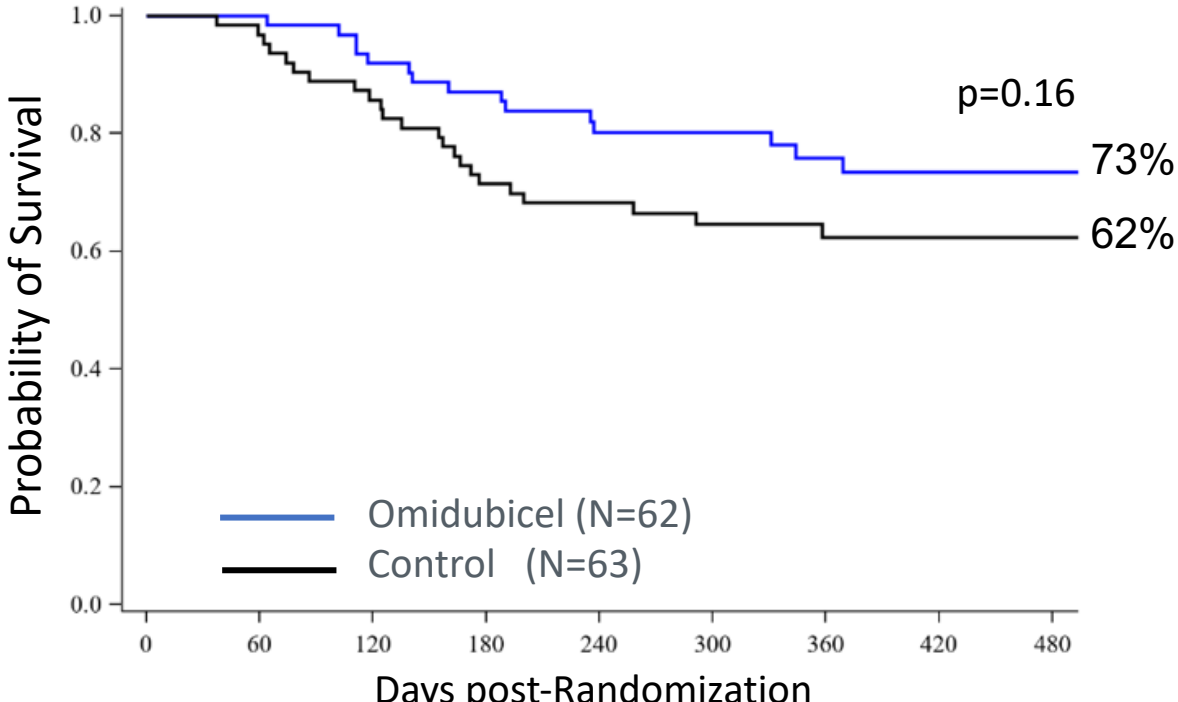
Summary and Conclusion

- Myeloablative transplantation with omidubicel results in
  - Faster hematopoietic recovery
  - Fewer early infections
  - Fewer days in the hospital
- No excessive toxicity associated with omidubicel compared to standard umbilical cord blood transplantation
  - Durable engraftment >10yrs (earlier studies)
- Omidubicel should be considered a new standard of care for patients eligible for umbilical cord blood transplantation

Acknowledgments

Co-Investigators

Patrick Stiff
Corey Cutler
Claudio Brunstein
Rabi Hanna
Richard Maziarz
Andrew Rezvani
Nicole Karras
Joseph McGuirk
Gary Schiller
Christine Duncan
Amy Keating
Yasser Khaled
Olga Frankfurt
Victor Aquino
Joanne Kurtzberg

Edward Peres
Dennis Cooper
Leonid Volodin
Guillermo Sanz
David Valcarcel
Isabel Badell
William Hwang
Liang Pui Koh
Caroline Lindemans
Nelson Hamerschlak
Vanderson Rocha
Juliana Folloni
Ron Ram
Moshe Yeshurun
Robert Wynn
Emma Nicholson

Gamida Cell

Tony Peled, PhD; Founder and Inventor
Einat Galamidi-Cohen, MD
Irit Segalovich

Emmes Corp.

Steven Wease
Beth Blackwell

Laurence Freedman, PhD (Statistics)

Patients and their families who participated in the Study