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

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Umbilical cord blood stem cell grafts

Advantages

- Readily available stem cells source
- Tolerance across HLA barriers
- Less chronic GvHD vs. Matched Unrelated donor
- Potent anti-tumor activity

Disadvantages

- **Low stem cell dose**
  - **Delayed hematopoietic recovery**
    - *Increased transplant-related morbidity and mortality*
    - *Increased hospital resource utilization*
  - Delayed immune recovery

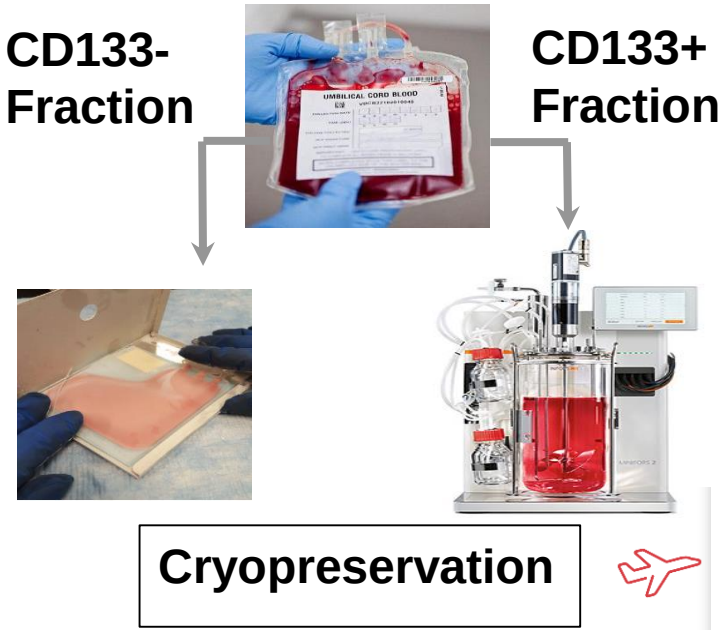
Potential solution
***Ex-vivo* expansion of cord blood stem cells**

Omidubicel

Cellular product consisting of two cryopreserved fractions derived from a single entire cord blood unit (CBU) and thawed at the transplant center immediately before infusion

- Cells obtained after CD133+ selection *ex vivo* expanded for 21 days in the presence of nicotinamide*
- Non-cultured CD133- cells, including T cells

*__Nicotinamide__ increases stem and progenitors cells, inhibits differentiation and increases migration, BM homing, and engraftment efficiency while preserving cellular functionality & phenotype



Omidubicel: phase I/II trial (N=36)

Patients: 36 patients with high-risk hematologic malignancies (78% with intermediate/high DRI) undergoing myeloablative conditioning

UCB grafts:

- **CD34+ cells infused (median): 6.3 x 10^6/kg**

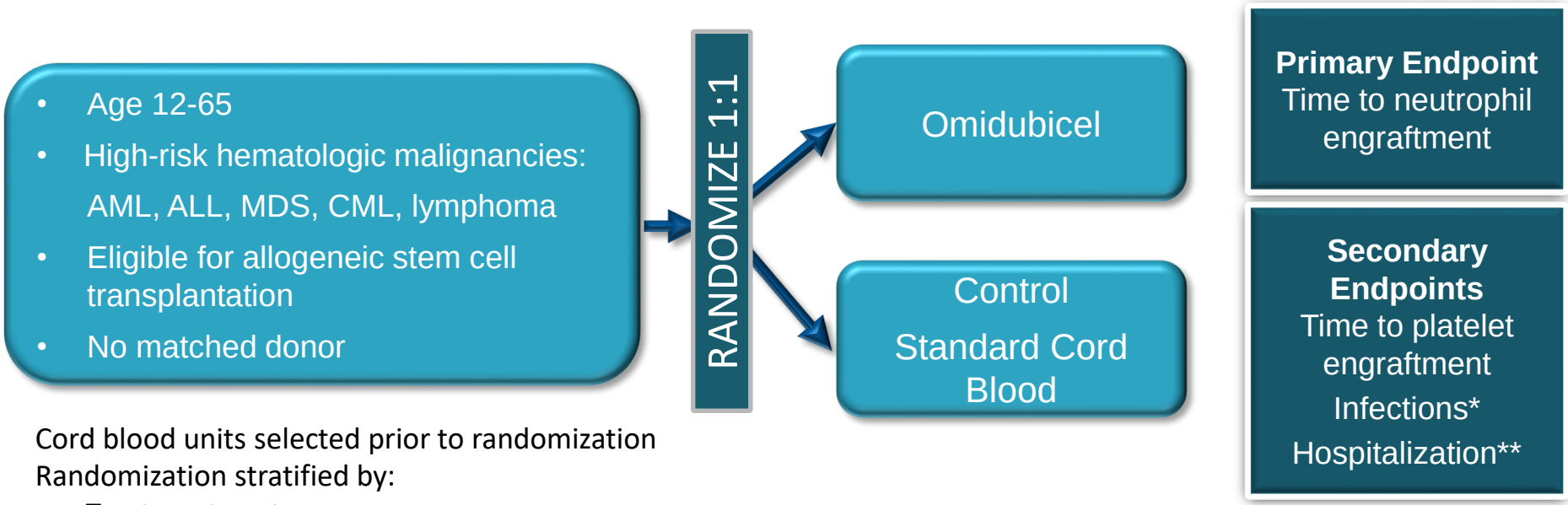
Results

- **Very fast hematopoietic engraftment**
  - Median time to neutrophil engraftment, days: 11.5*
  - Median time to platelet engraftment, days: 34*
  - Median days alive & out of hospital before day +100: 73*
- **Durable long-term hematopoietic engraftment** (>10 years)

* *P* < .001 as compared to 146 similar patients reported to the CIBMTR

Horwitz ME, et al. *J Clin Oncol*. 2019; 37(5): 367 – 374. [5]

Phase 3 trial of omidubicel



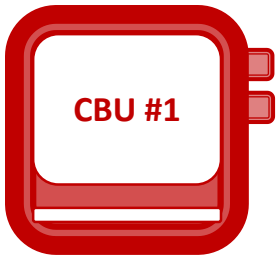
Cord blood units selected prior to randomization
Randomization stratified by:

- Treatment center
- Disease risk index
- Age
- Intent to perform single vs double cord transplant in the control arm

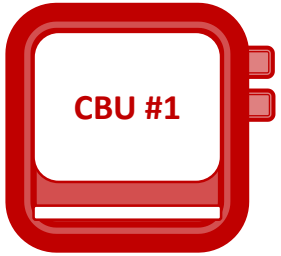
* Grade 2/3 bacterial or invasive fungal infections by 100 days post transplant
** Days alive and out of the hospital in the first 100 days post transplant

CBU selection criteria

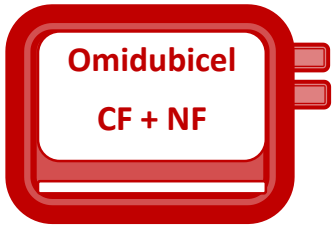
Omidubicel ← **Randomization** → **Standard Cord**



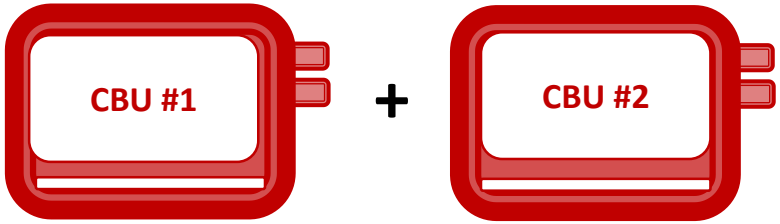
4-6/6 HLA Match
TNC count ≥ 1.8×10^9 cells
TNC dose ≥ 1.5×10^7 cells/kg
CD34⁺ count ≥ 8×10^6 cells
Red cell and plasma reduced
At least 1 allele match at DRB1



Production

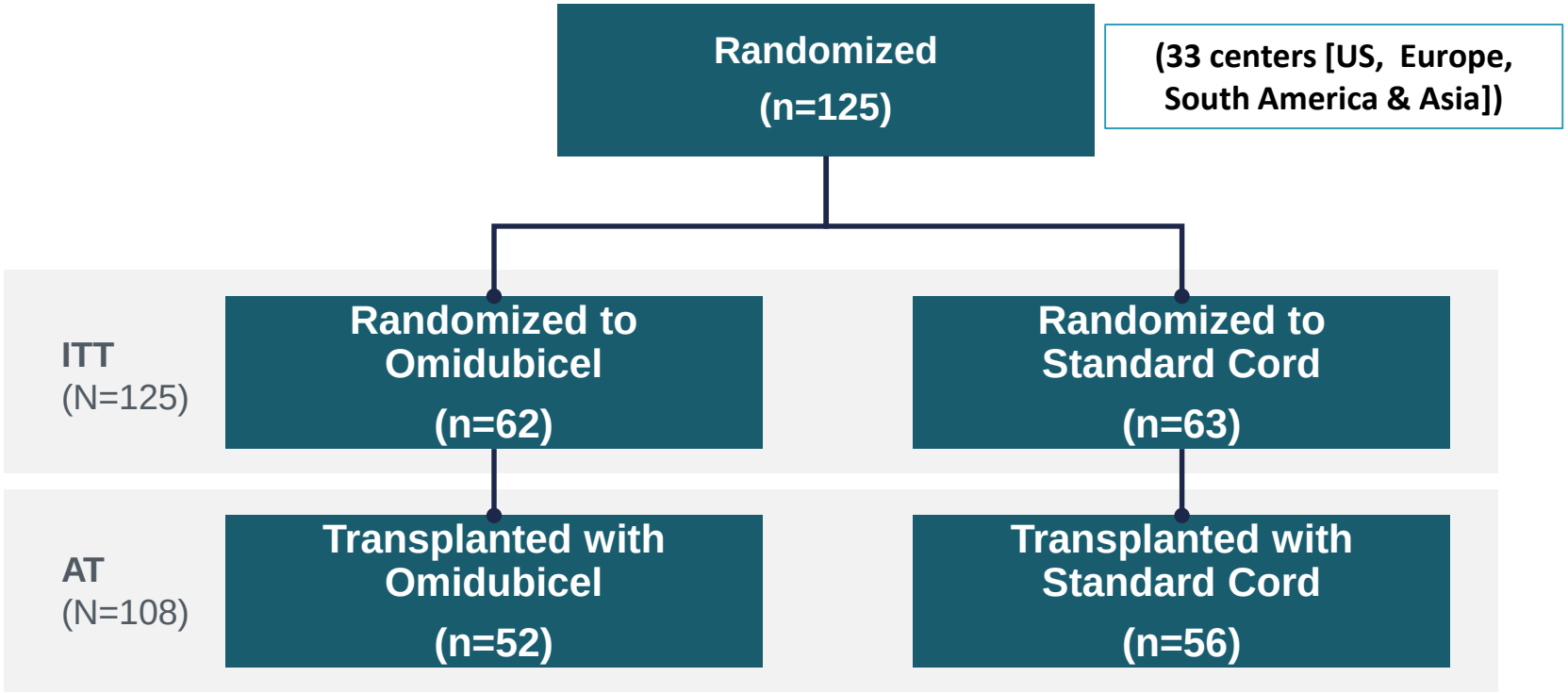


OR
(per EBMT 2006 CBU selection guidelines)*



*** 5 – 6/6 HLA match: TNC dose** < 2.5×10^7 cells/kg OR **CD34⁺ dose** < 1.2×10^5 cells/kg
4 – 6/6 HLA match: **TNC dose** < 3.5×10^7 cells/kg OR **CD34⁺ dose** < 1.7×10^5 cells/kg

Patient disposition



ITT: Intent to treat; AT: As treated population (received transplantation with omidubicel or standard cord per protocol)

Demographics

		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%)

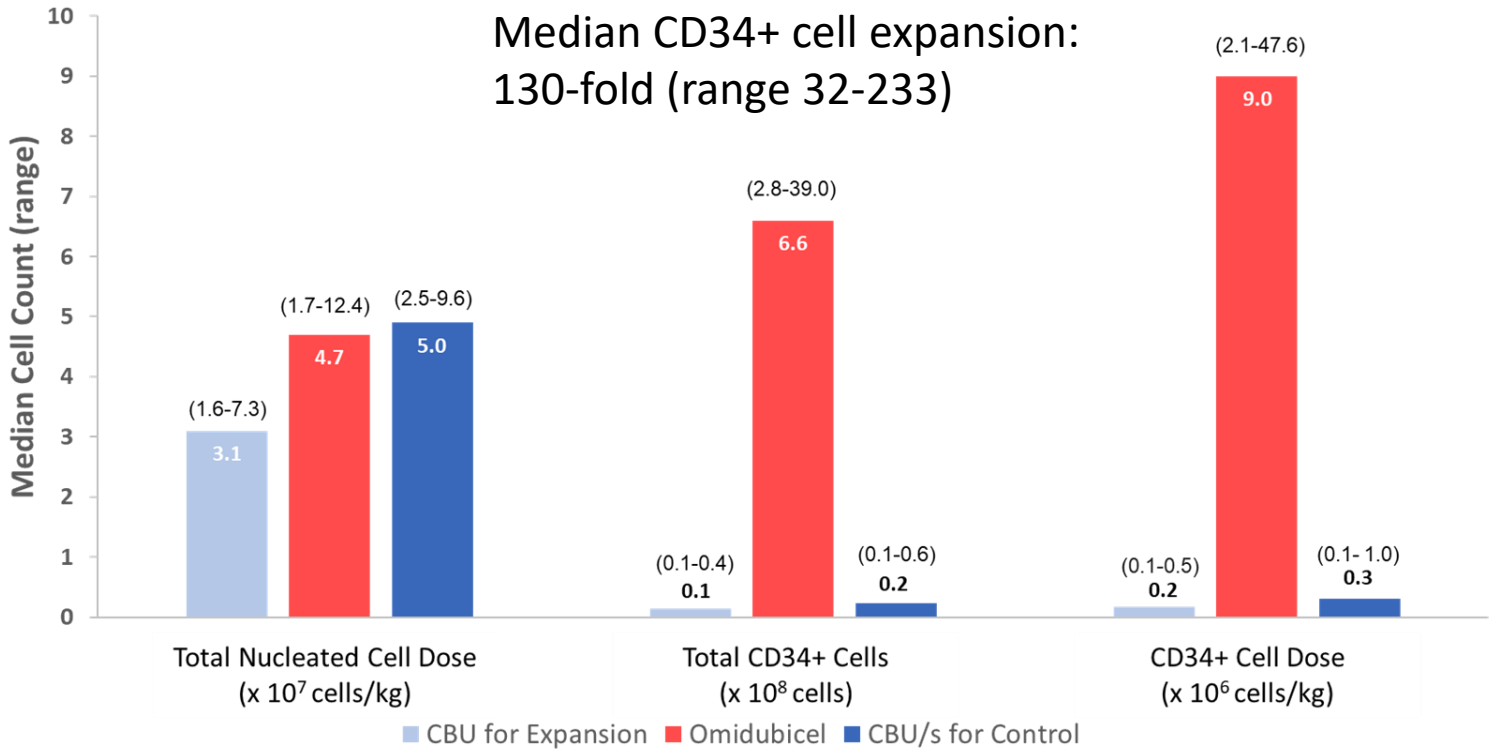
Patient and transplant characteristics

		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%)
Disease Risk Index	Low	15 (24%)	15 (24%)
	Moderate	27 (44%)	25 (40%)
	High/Very High	20 (32%)	23 (37%)
Myeloablative Conditioning Regimen	TBI, Fludarabine, Cyclophosphamide or Thiotepa	31 (50%)	30 (47%)
	Thiotepa, Busulfan, Fludarabine	27 (44%)	28 (44%)

Graft characteristics: HLA match & intended number of CBUs to be transplanted

		Omidubicel (N=62)	Control (N=63)
HLA match (CBU #1)	4/6	46 (74%)	46 (73%)
	5/6	15 (24%)	16 (25%)
	6/6	1 (2%)	1 (2%)
HLA match (CBU #2)	4/6		31 (74%)
	5/6		10 (24%)
	6/6		1 (2%)
Intended CBU transplant	Single	20 (32%)	21 (33%)
	Double	42 (68%)	42 (67%)

Graft characteristics: cell dose

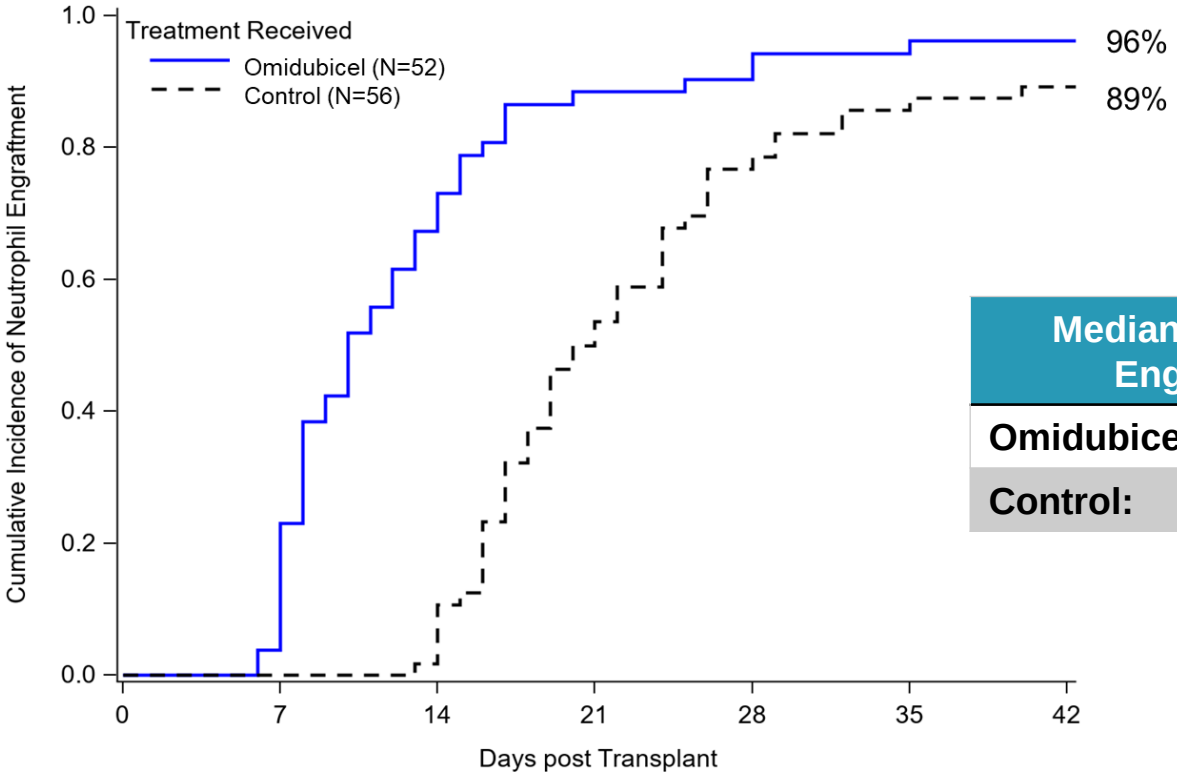


Primary endpoint
Time to neutrophil engraftment (ITT population)

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

*Patients not transplanted or who did not engraft by Day 42 post transplant were assigned Day 43
**Mann-Whitney test

Neutrophil engraftment (treated population, N = 108)

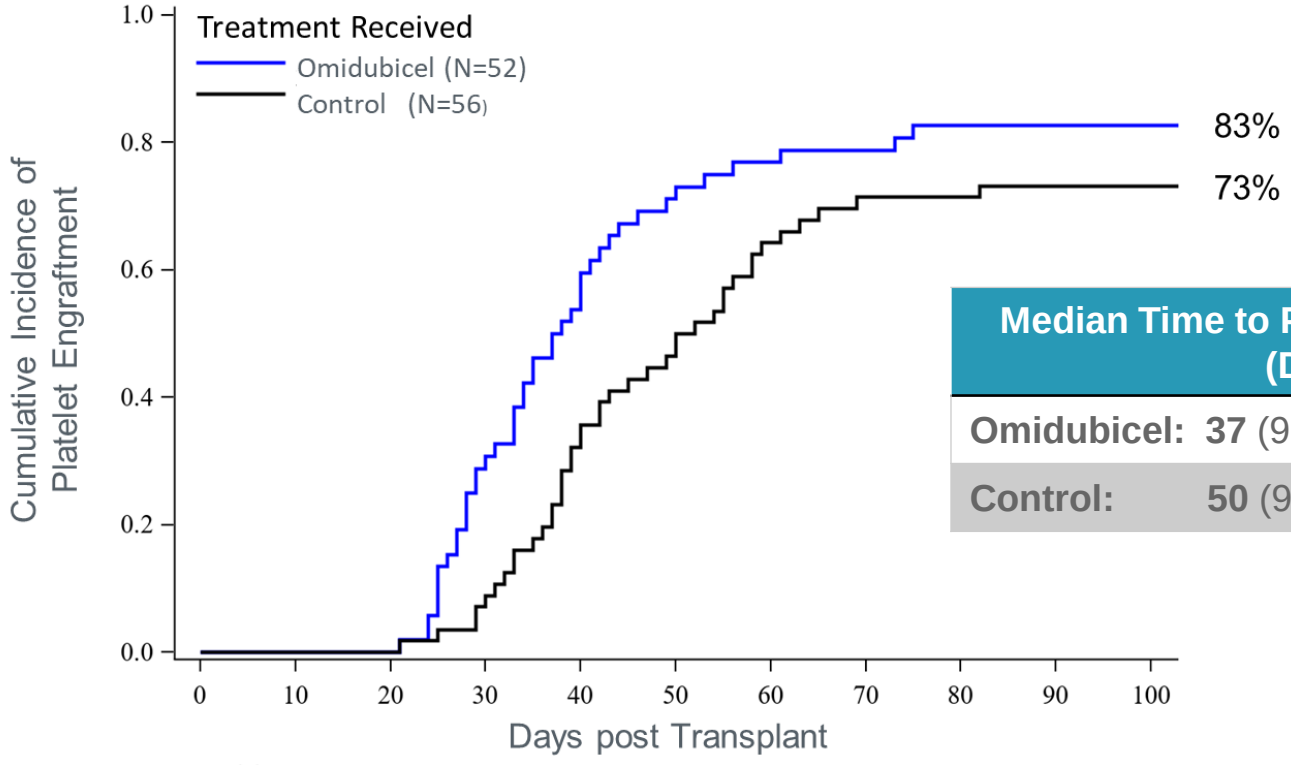


Median Time to Neutrophil Engraftment (Days)	P value
Omidubicel: 10.0 (95% CI: 8, 13)	**p<0.001**
Control: 20.5 (95%CI: 18, 24)	

Secondary endpoint:
Time to platelet engraftment (ITT population)

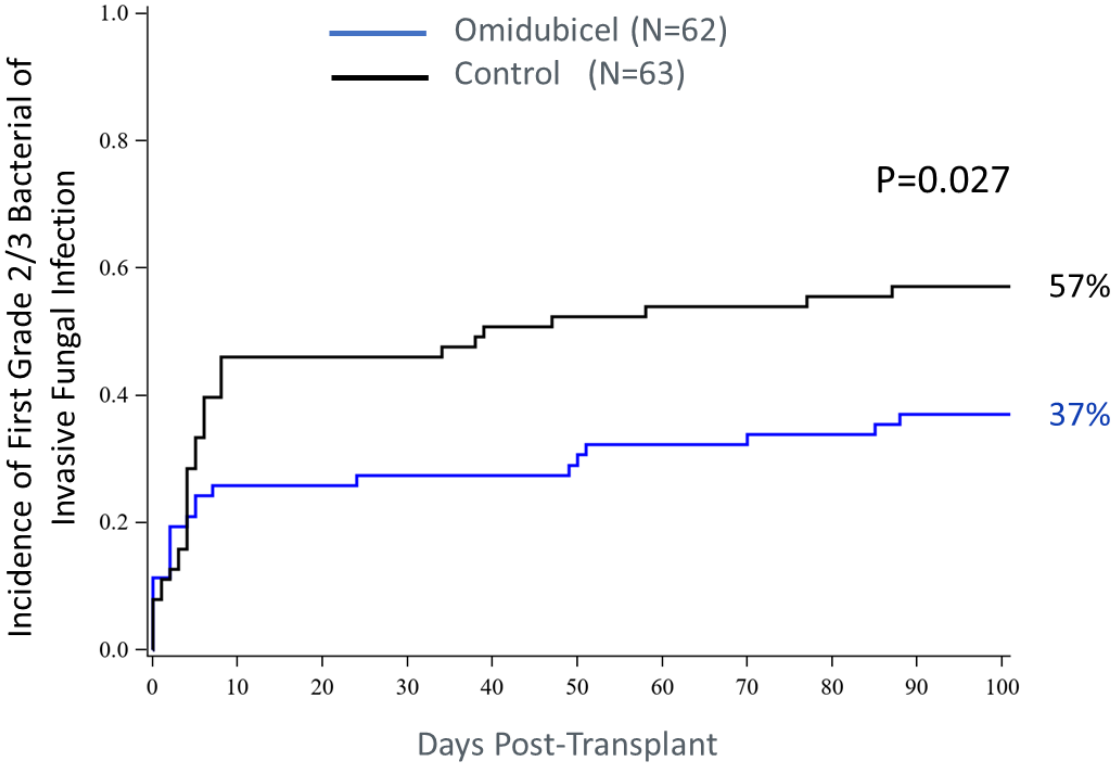
Intent-to-treat	Cumulative Day 42 Incidence	Difference in Cumulative Incidence	95% CI	P Value
Omidubicel (N = 62)	**0.55**	0.20	(0.03 – 0.35)	**0.028**
Control (N = 63)	**0.35**			

Platelet engraftment (treated population, N = 108)

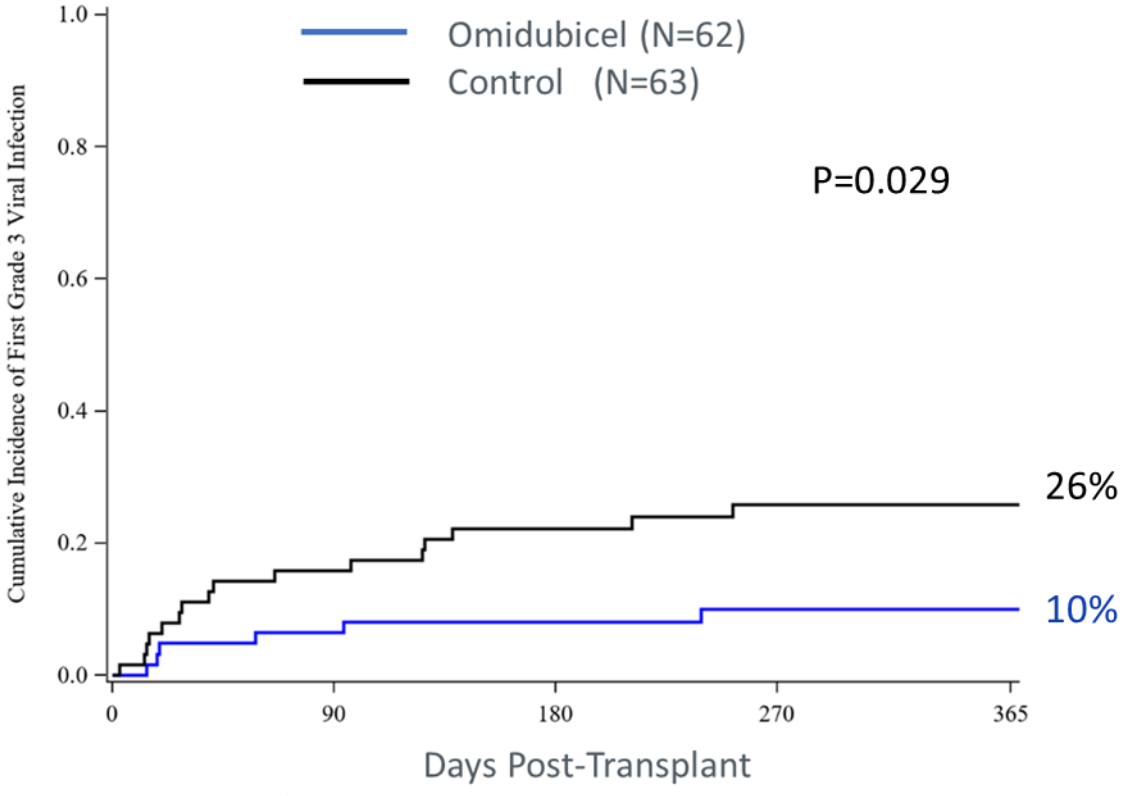


Median Time to Platelet Engraftment (Days)	P value
Omidubicel: **37** (95% CI: 33, 42)	**P=0.023**
Control: **50** (95%CI: 42, 58)	

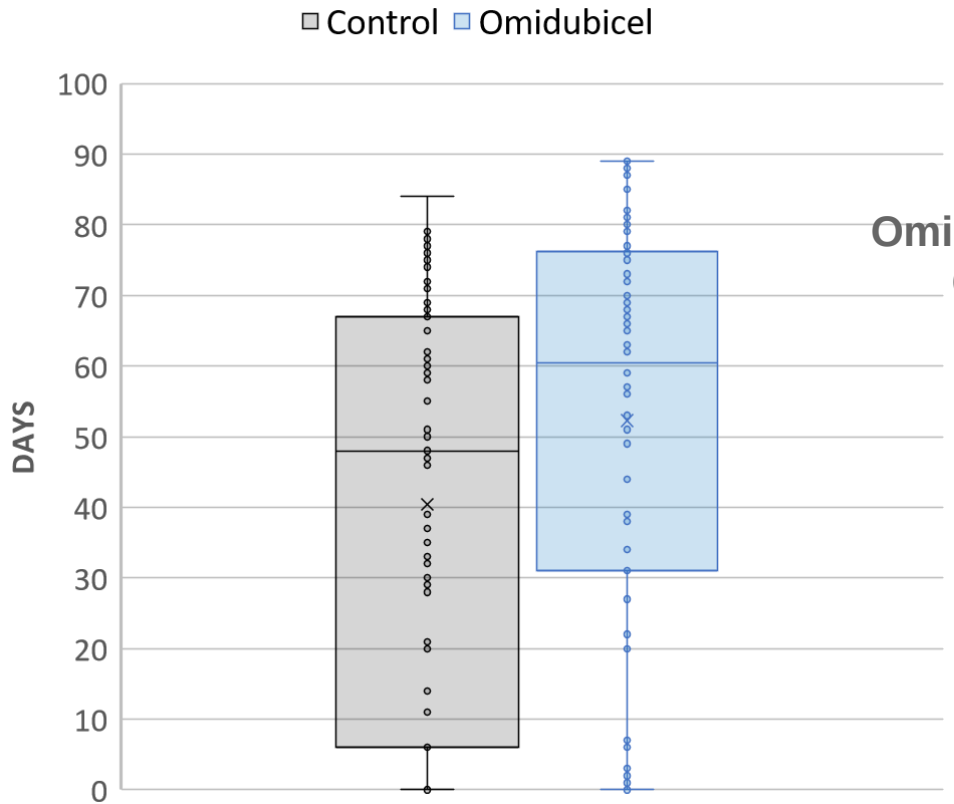
Secondary endpoint: Grade 2-3 bacterial or invasive fungal infection by 100 days (ITT Population)



Viral infections (ITT population)



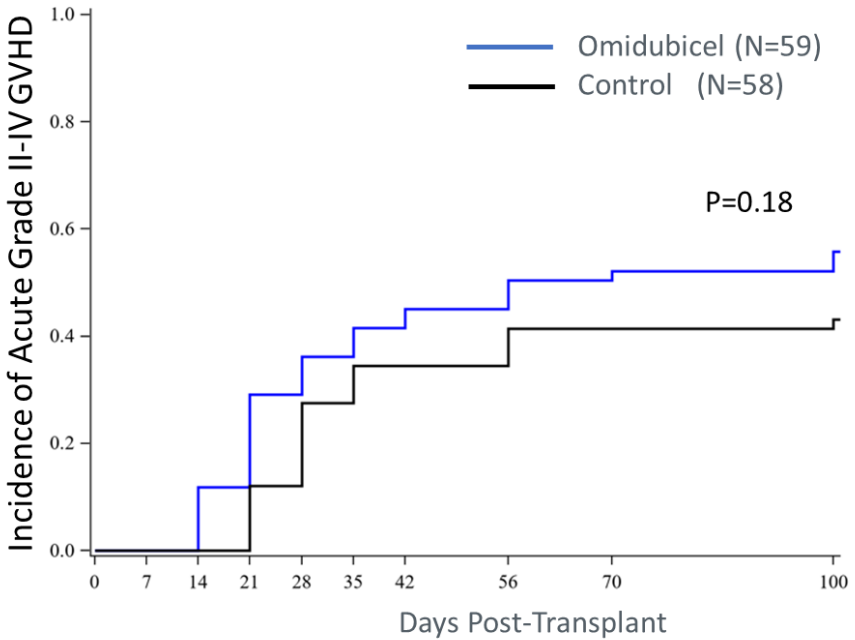
Secondary endpoint: Days alive and out of the hospital in the first 100 days post-transplant (ITT)



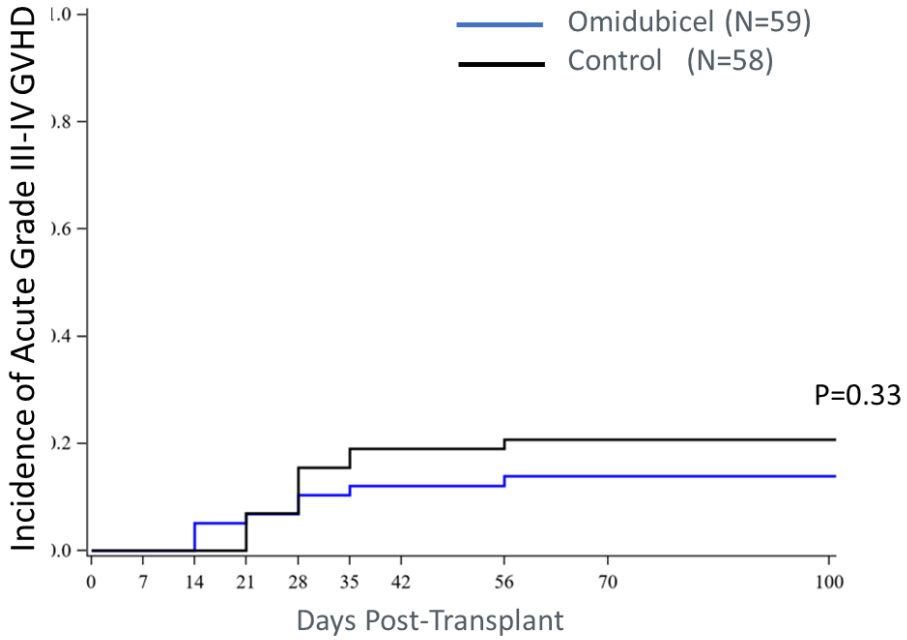
Omidubicel: Median **60.5** days
Control: Median **48.0** days
***P* = 0.005**

Acute GvHD

Grade II-IV Acute GVHD Day 100

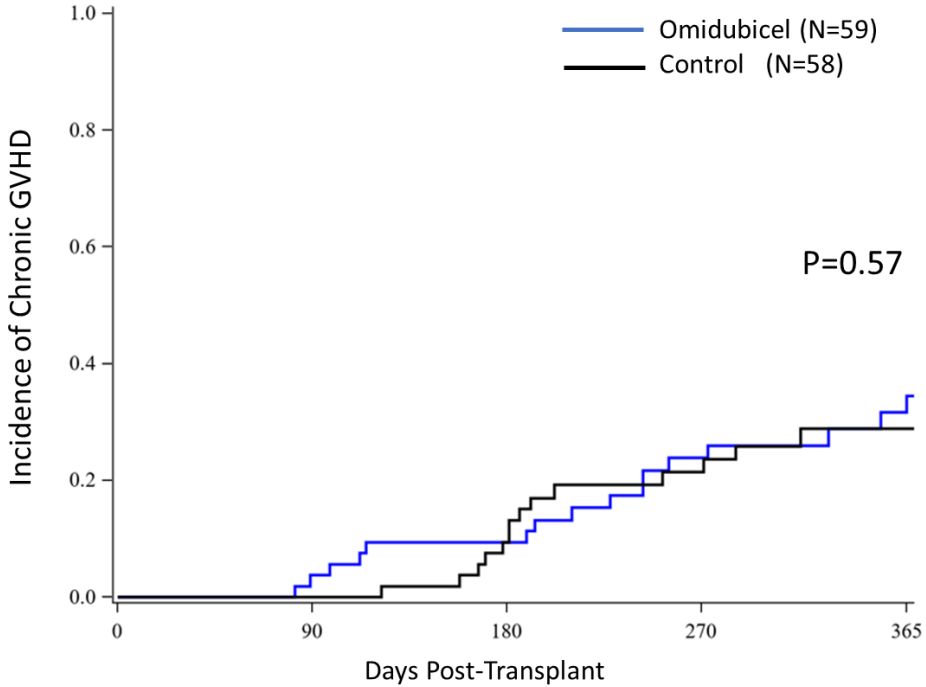


Grade III-IV Acute GVHD Day 100



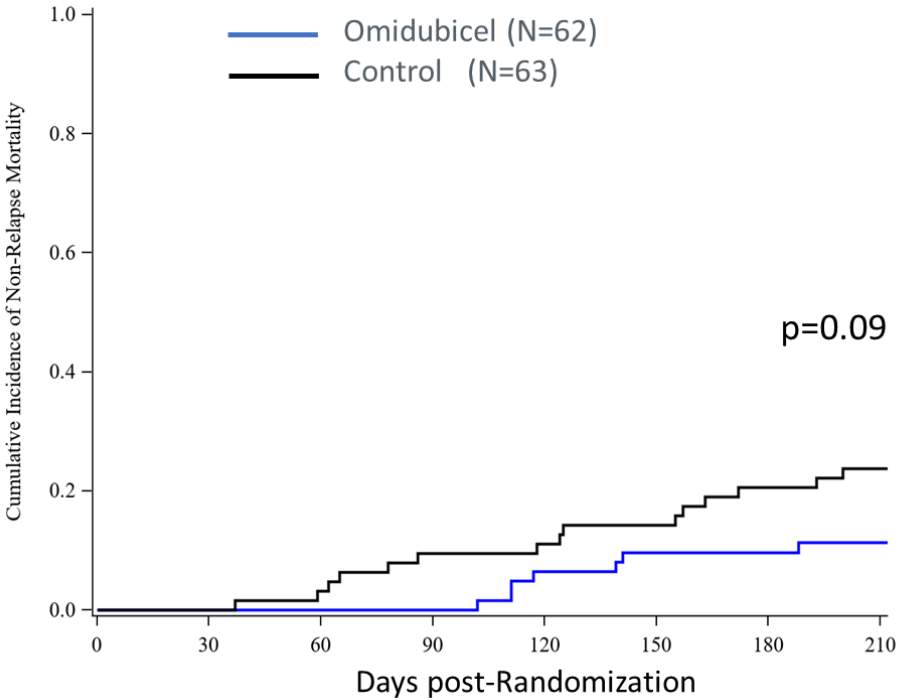
Chronic GvHD

All Chronic GVHD at One Year

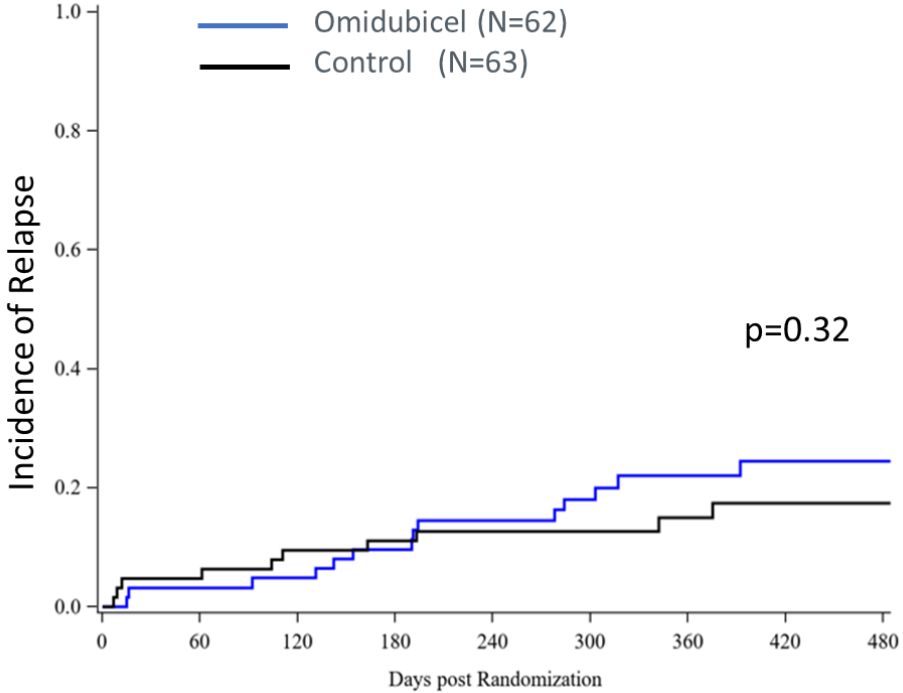


Non-relapse mortality and relapse (ITT)

Non-Relapse Mortality

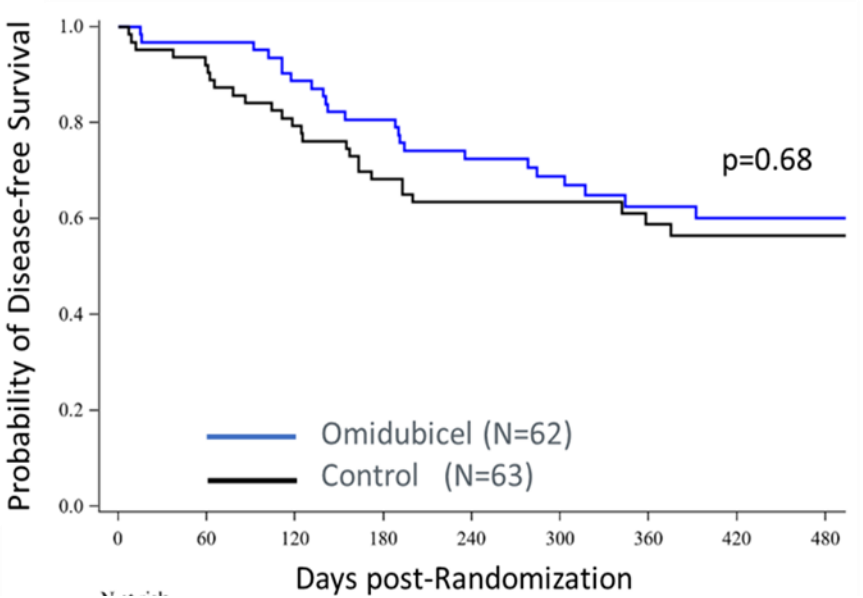


Relapse

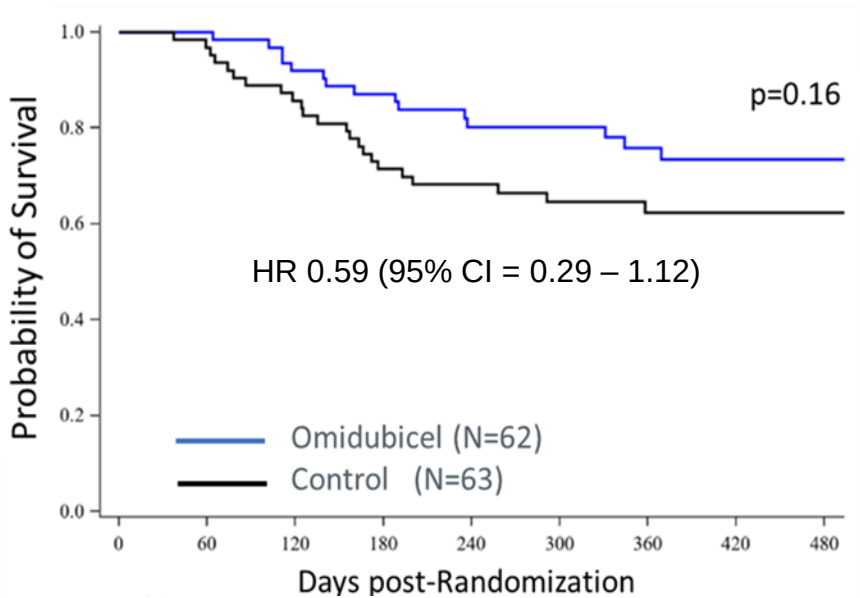


Disease-free and overall survival (ITT)

Disease-Free Survival



Overall Survival



Conclusions

- This global phase III randomized study demonstrated that transplantation with omidubicel compared to standard cord blood transplantation results in
  - Faster hematopoietic recovery
  - Fewer infections
  - Fewer days in hospital
- Omidubicel should be considered as the new standard of care for patients eligible for UCBT

Acknowledgements

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EBMT