

# Supplementary Appendix

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## Supplemental Section 1: CIBMTR Data Source

The CIBMTR is a working group of more than 500 transplantation centers worldwide that contribute detailed data on HCT to a statistical center at the Medical College of Wisconsin (MCW). Participating centers are required to report all transplantations consecutively and compliance is monitored by on-site audits. Computerized checks for discrepancies, physicians' review of submitted data, and on-site audits of participating centers ensure data quality.

Observational studies conducted by the CIBMTR are performed in compliance with all applicable federal regulations pertaining to the protection of human research participants. The MCW and National Marrow Donor Program, Institutional Review Boards approved this study.

The CIBMTR collects data at two levels: Transplant Essential Data (TED) and Comprehensive Report Form (CRF) data. TED-data includes disease type, age, gender, pre-HCT disease stage and chemotherapy-responsiveness, date of diagnosis, graft type, conditioning regimen, post-transplant disease progression and survival, development of a new malignancy, and cause of death. All CIBMTR centers contribute TED-data. More detailed disease and pre- and post-transplant clinical information is collected on a subset of registered patients selected for CRF data by a weighted randomization scheme. TED- and CRF-level data are collected pre-transplant, 100-days, and six months post-HCT and annually thereafter or until death. Data for the current analysis were retrieved from CIBMTR (TED and CRF) report forms.

## Supplemental Table 1: Variables tested in Cox proportional hazards regression model

### Main effect:

- **Patient age at HCT**, 55-64 vs. ≥65

### Patient-related:

- **Patient sex**: male vs. female
- **Karnofsky performance status** at transplant: ≥90 vs. <90 vs missing
- **HCT comorbidity index** at transplant: 0 vs 1-2 vs. ≥ 3 vs missing
- **Patient race**: Caucasian vs. other

### Disease-related:

- **Diagnosis**: FL vs. DLBCL vs MCL vs Mature T/NK cell lymphoma vs NHL others
- **Chemosensitivity status prior to HCT**: chemosensitive vs. refractory vs. untreated/unknown
- **History of autologous transplant**: No vs. Yes
- **Time from diagnosis to HCT**: >24 months vs. ≤24 months

### Transplant-related:

- **Graft source**: peripheral blood vs bone marrow
- **Transplant donor type**: Matched related vs matched unrelated (8/8) vs mismatched unrelated
- **GVHD prophylaxis**: CNI+MTX+others vs CNI+MMF+others vs CNI + other(s) except MMF, MTX, post CY vs. Others vs. missing
- **Donor-Recipient CMV match**: Donor+/Recipient – vs. others vs. missing
- **ATG/alemtuzumab**: no vs. yes vs. missing
- **Year of transplant**: continuous

Supplemental Table 2: Complete Multivariable Analysis Results

	N	RR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
<b>Non-relapse mortality</b>						
<b>Main effect</b>						
<b>Age</b>						
55-64	1166	1				0.02
≥65	436	1.29	1.04	1.61	0.02	
<b>Karnofsky performance score</b>						
≥90	965	1				<.0001
<90	571	1.52	1.24	1.88	<.0001	
Missing	66	1.54	0.94	2.53	0.09	
<b>HCT-CI</b>						
0	489	1				<.0001
1 -2	480	1.04	0.78	1.38	0.78	
≥3	617	1.63	1.27	2.10	0.0001	
Missing	16	0.68	0.21	2.21	0.52	
<b>Prior auto</b>						
No	1022	1				0.002
Yes	580	1.39	1.13	1.71	0.002	
<b>Donor type &amp; ATG/Campath</b>						
Matched related donor and ATG/Campath = No	609	1				<.0001
Matched related donor and ATG/Campath = Yes	79	1.54	0.93	2.54	0.09	
Matched unrelated donor and ATG/Campath = No	438	1.48	1.13	1.93	0.004	
Matched unrelated donor and ATG/Campath = Yes	301	1.54	1.14	2.07	0.005	
Mismatched unrelated donor and ATG/Campath = No	109	1.96	1.36	2.84	.0003	
Mismatched unrelated donor and ATG/Campath = Yes	66	2.75	1.78	4.24	<.0001	
<b>Relapse</b>						
<b>Main Effect</b>						
<b>Age</b>						
55-64	1166	1				0.80

	N	RR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
≥65	436	1.02	0.86	1.22	0.80	
<b>Subtype of lymphoma</b>						
Follicular	350	1				<.0001
DLBCL	479	1.89	1.48	2.42	<.0001	
Mantle cell	382	1.75	1.36	2.25	<.0001	
Mature T/NK-cell	321	1.93	1.49	2.51	<.0001	
NHL, other	70	1.20	0.76	1.88	0.44	
<b>Time from diagnosis to transplant</b>						
>24 months	1018	1				0.003
≤24 months	584	1.28	1.09	1.51	0.003	
<b>Race</b>						
Caucasian	1495	1				0.021
Other	107	1.39	1.05	1.84	0.02	
<b>Disease status (≤12 months)</b>						
Sensitive	1366	1				<.0001
Resistant	236	2.50	2.03	3.09	<.0001	
<b>Disease status (&gt;12 months)</b>						
Sensitive	766	1				0.33
Resistant	74	0.76	0.44	1.32	0.33	
<b>GVHD prophylaxis (≤18 months)</b>						
CNI + MTX + other(s) except MMF, post CY	767	1				0.49
CNI + MMF + other(s) except post CY	544	1.09	0.90	1.32	0.38	
CNI + other(s) except MMF, MTX, post CY	190	0.89	0.66	1.18	0.41	
Others	101	0.90	0.62	1.32	0.60	
<b>GVHD prophylaxis (&gt;18 months)</b>						
CNI + MTX + other(s) except MMF, post CY	333	1				<.0001
CNI + MMF + other(s) except post CY	225	0.90	0.61	1.34	0.61	
CNI + other(s) except MMF, MTX, post CY	87	0.97	0.53	1.76	0.91	
Others	41	3.59	2.06	6.28	<.0001	
<b>Progression-free survival</b>						

	N	RR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
<b>Main effect</b>						
<b>Age</b>						
55-64	1166	1				0.14
≥65	436	1.11	0.97	1.27	0.14	
<b>Karnofsky score</b>						
≥90	965	1				0.003
<90	571	1.25	1.10	1.43	0.0007	
Missing	66	1.14	0.83	1.55	0.43	
<b>HCT-CI</b>						
0	489	1				0.007
1 -2	480	1.07	0.91	1.26	0.43	
≥3	617	1.29	1.10	1.50	0.001	
Missing	16	0.92	0.48	1.76	0.80	
<b>Subtype of lymphoma</b>						
Follicular	350	1				<.0001
DLBCL	479	1.64	1.36	1.97	<.0001	
Mantle cell	382	1.49	1.23	1.80	<.0001	
Mature T/NK-cell	321	1.58	1.30	1.93	<.0001	
NHL, other	70	1.24	0.89	1.73	0.20	
<b>Donor type &amp; ATG/Campath</b>						
Matched related donor and ATG/Campath = No	609	1				0.023
Matched related donor and ATG/Campath = Yes	79	1.20	0.89	1.61	0.23	
Matched unrelated donor and ATG/Campath = No	438	1.00	0.85	1.18	0.98	
Matched unrelated donor and ATG/Campath = Yes	301	1.15	0.97	1.37	0.12	
Mismatched unrelated donor and ATG/Campath = No	109	1.01	0.78	1.30	0.96	
Mismatched unrelated donor and ATG/Campath = Yes	66	1.60	1.19	2.13	0.002	
<b>Disease status ( ≤12 months)</b>						
Sensitive	1366	1				<.0001
Resistant	236	2.05	1.71	2.45	<.0001	

	N	RR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
<b>Disease status (&gt;12 months)</b>						
Sensitive	766	1				0.58
Resistant	74	0.90	0.60	1.33	0.58	
<b>GVHD prophylaxis (≤18 months)</b>						
CNI + MTX + other(s) except MMF, post CY	767	1				0.24
CNI + MMF + other(s) except post CY	544	1.13	0.96	1.32	0.13	
CNI + other(s) except MMF, MTX, post CY	190	0.90	0.71	1.14	0.36	
Others	101	1.03	0.76	1.38	0.86	
<b>GVHD prophylaxis (&gt;18 months)</b>						
CNI + MTX + other(s) except MMF, post CY	333	1				<.0001
CNI + MMF + other(s) except post CY	225	1.04	0.76	1.42	0.80	
CNI + other(s) except MMF, MTX, post CY	87	1.69	1.14	2.52	0.01	
Others	41	3.45	2.15	5.52	<.0001	
<b>Overall survival</b>						
<b>Main effect</b>						
<b>Age</b>						
55-64	1166	1				0.10
≥65	436	1.14	0.97	1.33	0.10	
<b>Karnofsky performance score</b>						
≥90	965	1				0.0007
<90	571	1.34	1.15	1.56	0.0001	
Missing	66	1.11	0.78	1.58	0.56	
<b>HCT-CI</b>						
0	489	1				0.001
1 -2	480	0.95	0.79	1.16	0.62	
≥3	617	1.30	1.09	1.55	0.003	
Missing	16	0.84	0.39	1.80	0.65	
<b>Subtype of lymphoma</b>						
Follicular	350	1				<.0001
DLBCL	479	1.86	1.50	2.31	<.0001	
Mantle cell	382	1.53	1.22	1.93	0.0002	
Mature T/NK-cell	321	1.48	1.17	1.88	0.001	
NHL, other	70	1.78	1.25	2.55	0.002	
<b>Disease status</b>						
Sensitive	1366	1				0.0002

	N	RR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
Resistant	236	1.43	1.19	1.73	0.0002	
<b>Donor type &amp; ATG/Campath</b>						
Matched related donor and ATG/Campath = No	609	1				0.02
Matched related donor and ATG/Campath = Yes	79	1.13	0.81	1.60	0.47	
Matched unrelated donor and ATG/Campath = No	438	1.08	0.90	1.30	0.41	
Matched unrelated donor and ATG/Campath = Yes	301	1.20	0.98	1.46	0.09	
Mismatched unrelated donor and ATG/Campath = No	109	1.19	0.89	1.58	0.24	
Mismatched unrelated donor and ATG/Campath = Yes	66	1.79	1.29	2.48	0.0005	



### Supplemental Table 3: Cause of Death

	55-64	≥65
<b>Total number of deaths</b>	550	232
<b>Primary disease</b>	212 (39)	79 (34)
<b>GVHD</b>	86 (16)	32 (14)
<b>Infection</b>	76 (14)	39 (17)
<b>Organ failure</b>	71 (13)	28 (12)
<b>Secondary malignancy</b>	20 (3)	4 (2)
<b>Interstitial Pneumonitis</b>	6 (1)	2 (1)
<b>Acute Respiratory Distress Syndrome</b>	1 (<1)	1 (<1)
<b>Graft rejection</b>	1 (<1)	2 (1)
<b>Hemorrhage</b>	4 (1)	2 (1)
<b>Other cause<sup>1</sup></b>	49 (9)	35 (15)
<b>Missing</b>	24 (4)	8 (3)

<sup>1</sup>Other causes: 55-64: 1 diffuse alveolar hemorrhage; 1 fludarabine toxicity; 1 hepatic encephalopathy; 1 lung cancer; 1 pleural effusion; 1 stroke; 2 sudden death; 1 suicide; 1 unknown; 1 autopsy declined by family; 38 NOS.

≥65: 1 TENS; 1 sudden death; 1 pulmonary embolism; 5 kidney disease; 1 neurologic disease; 1 metabolic encephalopathy; 1 ischemic stroke; 1 HLH; 1 deconditioning; 1 altered mental status; 1 ARDS; 1 aspiration pneumonia; 2 cardiac arrest; 1 failure to thrive from toxicity of prograf; 3 pneumonia; 1 progressive dementia; 1 respiratory distress; 1 uncal herniation; 1 uncharacterized neurodegenerative illness; 1 unknown; 8 NOS.