

Association between the choice of the conditioning regimen and outcomes of allogeneic hematopoietic cell transplantation for myelofibrosis

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Received: September 6, 2022.

Accepted: February 1, 2023.

Early view: February 9, 2023.

<https://doi.org/10.3324/haematol.2022.281958>

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Supplement:

Definition of outcomes:

Disease free survival was defined as time from allo-HCT to treatment failure (relapse or death from any cause).

Overall survival was defined as time from allo-HCT to death from any cause.

Acute GVHD ²⁶ and chronic GVHD ²⁷ were graded per standard criteria.

Relapse was defined as disease recurrence as reported by the centers to CIBMTR.

Non-relapse mortality was defined as death from any cause in the first 28 days after allo-HCT or death without evidence of disease recurrence beyond day 28.

GVHD-free relapse-free survival was defined as time from allo-HCT to death, post-transplant relapse, chronic GVHD requiring immunosuppressive treatment, or severe acute GVHD (aGVHD III-IV).

Supplemental Table S1. Baseline characteristics with reduced intensity conditioning

Characteristic	RIC: Flu/Bu	RIC: Flu/Mel	P Value
No. of patients	166	327	
Patient age - median (min-max)	63 (44-75)	63 (38-78)	0.88 ^a
Age group - no. (%)			0.50 ^b
30-39	0 (0)	1 (0)	
40-49	10 (6)	31 (9)	
50-59	43 (26)	77 (24)	
60-69	99 (60)	182 (56)	
>= 70	14 (8)	36 (11)	
Sex - no. (%)			0.40 ^b
Male	105 (63)	194 (59)	
Female	61 (37)	133 (41)	
Region - no. (%)			<.01 ^b
US	146 (88)	310 (95)	
Europe	12 (7)	2 (1)	
Australia/New Zealand	8 (5)	15 (5)	
Race/ethnicity - no. (%)			0.16 ^b
Hispanic	3 (2)	17 (5)	
Non-Hispanic White	150 (90)	274 (84)	
Non-Hispanic Black/African American	4 (2)	9 (3)	
Other	7 (4)	14 (4)	
Missing	2 (1)	13 (4)	
HCT-CI - no. (%)			0.13 ^b
0	23 (14)	72 (22)	
1	22 (13)	34 (10)	
2	29 (17)	52 (16)	
3	34 (20)	71 (22)	
4	24 (14)	40 (12)	
5	16 (10)	17 (5)	
6+	11 (7)	33 (10)	
Missing	7 (4)	8 (2)	
Karnofsky performance score - no. (%)			0.37 ^b
90-100	79 (48)	152 (46)	
< 90	85 (51)	164 (50)	
Missing	2 (1)	11 (3)	
Disease type- no. (%)			0.22 ^b
Primary Myelofibrosis	132 (80)	242 (74)	

Characteristic	RIC: Flu/Bu	RIC: Flu/Mel	P Value
Post polycythemia vera	14 (8)	45 (14)	
Post Essential thrombocythemia	20 (12)	40 (12)	
Time from diagnosis to HCT - median (min-max)	22 (3-393)	37 (-99-594)	0.02 ^a
Time from diagnosis to HCT - no. (%)			0.09 ^b
<6 months	32 (19)	44 (13)	
6-11 months	34 (20)	50 (15)	
>=12 months	100 (60)	232 (71)	
Missing	0 (0)	1 (0)	
DIPSS Score - no. (%)			0.07 ^b
Low/Intermediate-1	71 (43)	107 (33)	
Intermediate-2/High	69 (42)	168 (51)	
Missing	26 (16)	52 (16)	
Splenomegaly at HCT - no. (%)			0.21 ^b
No	66 (40)	107 (33)	
Yes	82 (49)	168 (51)	
Splenectomy	8 (5)	16 (5)	
Missing	10 (6)	36 (11)	
Systemic symptoms prior to HCT. - no. (%)			0.19 ^b
No	137 (83)	252 (77)	
Yes	19 (11)	58 (18)	
Missing	10 (6)	17 (5)	
Donor type - no. (%)			0.75 ^b
HLA-identical sibling	48 (29)	94 (29)	
8/8 matched unrelated donor	107 (64)	205 (63)	
7/8 matched unrelated donor	11 (7)	28 (9)	
Donor/recipient sex match - no. (%)			0.81 ^b
Male-Male	71 (43)	135 (41)	
Male-Female	39 (23)	81 (25)	
Female-Male	34 (20)	58 (18)	
Female-Female	21 (13)	52 (16)	
Missing	1 (1)	1 (0)	
Donor/recipient CMV serostatus - no. (%)			0.73 ^b
+/+	54 (33)	102 (31)	
+/-	25 (15)	41 (13)	
-/+	39 (23)	70 (21)	
-/-	47 (28)	111 (34)	
Missing	1 (1)	3 (1)	
Graft type - no. (%)			0.84 ^b

Characteristic	RIC: Flu/Bu	RIC: Flu/Mel	P Value
Bone marrow	6 (4)	13 (4)	
Peripheral blood	160 (96)	314 (96)	
GVHD prophylaxis - no. (%)			<.01 ^b
Post-CY + other(s)	7 (4)	9 (3)	
TAC + MMF +/- other(s) (except post-CY)	28 (17)	36 (11)	
TAC + MTX +/- other(s) (except MMF, post-CY)	86 (52)	207 (63)	
TAC + other(s) (except MMF, MTX, post-CY)	7 (4)	36 (11)	
TAC alone	4 (2)	6 (2)	
CSA + MMF +/- other(s) (except post-CY)	4 (2)	2 (1)	
CSA + MTX +/- other(s) (except MMF, post-CY)	23 (14)	24 (7)	
CSA + other(s) (except MMF, MTX, post-CY)	0 (0)	1 (0)	
CSA alone	1 (1)	5 (2)	
Other(s)	6 (4)	1 (0)	
ATG/alemtuzumab use - no. (%)			<.01 ^b
No	79 (48)	246 (75)	
Yes	87 (52)	81 (25)	
ATG/Alemtuzumab - no. (%)			<.01 ^b
ATG alone	86 (52)	72 (22)	
Alemtuzumab alone	1 (1)	9 (3)	
No ATG or alemtuzumab	79 (48)	246 (75)	
ATG dose (mg) - median (min-max)	400 (5-4900)	284 (4-2988)	<.01 ^a
ATG dose (mg) - no. (%)			0.43 ^b
0-5mg	2 (2)	4 (6)	
5-7.5mg	2 (2)	0 (0)	
>7.5mg	78 (91)	65 (90)	
Missing	4 (5)	3 (4)	
Melphalan dose - no. (%)			
Melphalan 100mg/m ²	-	52 (16)	
Melphalan 140mg/m ²	-	275 (84)	
Busulfan Administration - no. (%)			
Oral	7 (4)	-	
IV	159 (96)	-	
Ruxolitinib use prior to HCT- no. (%)			0.03 ^b
No	84 (51)	125 (38)	
Yes	82 (49)	201 (61)	
Missing	0 (0)	1 (0)	
Splenic radiation prior HCT - no. (%)			0.36 ^b
No	161 (97)	308 (94)	
Yes	5 (3)	18 (6)	

Characteristic	RIC: Flu/Bu	RIC: Flu/Mel	P Value
Missing	0 (0)	1 (0)	
Year of HCT - no. (%)			0.01 ^b
2008	11 (7)	17 (5)	
2009	9 (5)	14 (4)	
2010	4 (2)	2 (1)	
2011	0 (0)	1 (0)	
2012	0 (0)	1 (0)	
2013	4 (2)	4 (1)	
2014	27 (16)	23 (7)	
2015	11 (7)	20 (6)	
2016	21 (13)	32 (10)	
2017	32 (19)	64 (20)	
2018	22 (13)	73 (22)	
2019	25 (15)	76 (23)	
Follow-up - median (range)	36 (3-143)	24 (3-122)	

Hypothesis testing: ^a Kruskal-Wallis test ^b Pearson chi-square test

Other race include: Asian (n= 15), Native Hawaiian or other Pacific Islander (n=4), More than 1 race (n=1)

RIC-Reduced intensity conditioning; Flu-Fludarabine; Bu-Busulfan; Mel- Melphalan; HCTCI-hematopoietic cell transplantation comorbidity index; HCT-hematopoietic cell transplantation; DIPSS- dynamic international prognostic scoring system; CMV – cytomegalovirus; TAC-tacrolimus, CSA – cyclosporine; MMF- mycophenolate mofetil; MTX- methotrexate; CY-cyclophosphamide; ATG – antithymocyte globulin; GVHD- graft versus host disease

Supplemental Table S2. Baseline characteristics with myeloablative conditioning

Characteristic	MAC: Flu/Bu	MAC: Bu/Cy	P Value
No. of patients	247	132	
No. of centers	61	30	
Patient age - median (min-max)	60 (27-74)	55 (24-67)	<.01 ^a
Age group - no. (%)			<.01 ^b
18-29	1 (0)	1 (1)	
30-39	2 (1)	7 (5)	
40-49	25 (10)	24 (18)	
50-59	96 (39)	78 (59)	
60-69	110 (45)	22 (17)	
>= 70	13 (5)	0 (0)	
Sex - no. (%)			0.17 ^b
Male	126 (51)	77 (58)	
Female	121 (49)	55 (42)	
Region - no. (%)			0.62 ^b
US	240 (97)	130 (98)	
Canada	1 (0)	1 (1)	
Europe	2 (1)	0 (0)	
Australia/New Zealand	4 (2)	1 (1)	
Race/ethnicity - no. (%)			<.01 ^b
Hispanic	16 (6)	3 (2)	
Non-Hispanic White	209 (85)	113 (86)	
Non-Hispanic Black/African American	15 (6)	3 (2)	
Other	7 (3)	10 (8)	
Missing	0 (0)	3 (2)	
HCTCI - no. (%)			0.32 ^b
0	62 (25)	45 (34)	
1	38 (15)	21 (16)	
2	40 (16)	19 (14)	
3	47 (19)	26 (20)	
4	31 (13)	13 (10)	
5	12 (5)	5 (4)	
6+	16 (6)	2 (2)	
Missing	1 (0)	1 (1)	
Karnofsky performance score - no. (%)			0.42 ^b
90-100	151 (61)	89 (67)	

Characteristic	MAC: Flu/Bu	MAC: Bu/Cy	P Value
< 90	92 (37)	42 (32)	
Missing	4 (2)	1 (1)	
Disease type - no. (%)			0.85 ^b
Primary Myelofibrosis	191 (77)	100 (76)	
Post polycythemia vera	20 (8)	13 (10)	
Post essential thrombocythemia	36 (15)	19 (14)	
Time from diagnosis to HCT - median (min-max)	25 (2-490)	38 (3-377)	0.41 ^a
Time from diagnosis to HCT - no. (%)			0.65 ^b
<6 months	38 (15)	24 (18)	
6-11 months	51 (21)	23 (17)	
≥12 months	158 (64)	85 (64)	
DIPSS Score - no. (%)			0.03 ^b
Low/Intermediate-1	134 (54)	80 (61)	
Intermediate-2/High	93 (38)	34 (26)	
Missing	20 (8)	18 (14)	
Splenomegaly at HCT - no. (%)			0.19 ^b
No	85 (34)	38 (29)	
Yes	133 (54)	73 (55)	
Splenectomy	10 (4)	12 (9)	
Missing	19 (8)	9 (7)	
Systemic symptoms prior to HCT- no. (%)			0.53 ^b
No	185 (75)	105 (80)	
Yes	51 (21)	21 (16)	
Missing	11 (4)	6 (5)	
Donor type - no. (%)			0.15 ^b
HLA-identical sibling	79 (32)	53 (40)	
8/8-matched unrelated	142 (57)	62 (47)	
7/8-matched unrelated	26 (11)	17 (13)	
Donor/recipient sex match - no. (%)			0.17 ^b
Male-Male	87 (35)	44 (33)	
Male-Female	72 (29)	31 (23)	
Female-Male	39 (16)	33 (25)	
Female-Female	49 (20)	24 (18)	
Donor/recipient CMV serostatus - no. (%)			0.37 ^b
+/+	66 (27)	26 (20)	
+/-	42 (17)	19 (14)	
-/+	64 (26)	40 (30)	

Characteristic	MAC: Flu/Bu	MAC: Bu/Cy	P Value
-/-	71 (29)	46 (35)	
Missing	4 (2)	1 (1)	
Graft type - no. (%)			<.01 ^b
Bone marrow	11 (4)	16 (12)	
Peripheral blood	236 (96)	116 (88)	
GVHD prophylaxis - no. (%)			0.03 ^b
TAC + MMF +/- other(s) (except post-CY)	26 (11)	5 (4)	
TAC + MTX +/- other(s) (except MMF, post-CY)	193 (78)	111 (84)	
TAC + other(s) (except MMF, MTX, post-CY)	12 (5)	3 (2)	
TAC alone	4 (2)	0 (0)	
CSA + MMF +/- other(s) (except post-CY)	3 (1)	2 (2)	
CSA + MTX +/- other(s) (except MMF, post-CY)	9 (4)	11 (8)	
ATG/Alemtuzumab use - no. (%)			<.01 ^b
No	135 (55)	125 (95)	
Yes	112 (45)	7 (5)	
ATG/alemtuzumab - no. (%)			<.01 ^b
ATG + alemtuzumab	1 (0)	0 (0)	
ATG alone	107 (43)	6 (5)	
Alemtuzumab alone	4 (2)	1 (1)	
No ATG or alemtuzumab	135 (55)	125 (95)	
ATG dose (mg) - median (min-max)	338 (3-6000)	250 (150-500)	0.32 ^a
ATG dose (mg) - no. (%)			0.10 ^c
0-5mg	3(3)	0(0)	
5-7.5mg	0(0)	0(0)	
>7.5mg	98(92)	4(67)	
Missing	6(6)	2(33)	
Busulfan pharmacokinetics performed - no. (%)			0.62 ^b
No	102 (41)	51 (39)	
Yes	145 (59)	81 (61)	
Busulfan Administration - no. (%)			0.02 ^b
Oral	2 (1)	6 (5)	
IV	245 (99)	126 (95)	
Ruxolitinib use prior to HCT - no. (%)			<.01 ^b
No	101 (41)	75 (57)	
Yes	146 (59)	57 (43)	
Splenic radiation prior HCT - no. (%)			0.07 ^b
No	237 (96)	131 (99)	

Characteristic	MAC: Flu/Bu	MAC: Bu/Cy	P Value
Yes	10 (4)	1 (1)	
Year of HCT - no. (%)			<.01 ^b
2008	9 (4)	15 (11)	
2009	12 (5)	21 (16)	
2010	5 (2)	8 (6)	
2011	2 (1)	6 (5)	
2012	1 (0)	3 (2)	
2013	9 (4)	6 (5)	
2014	35 (14)	6 (5)	
2015	27 (11)	15 (11)	
2016	25 (10)	11 (8)	
2017	47 (19)	15 (11)	
2018	39 (16)	15 (11)	
2019	36 (15)	11 (8)	
Follow-up - median (range)	25 (3-122)	49 (6-150)	

Hypothesis testing: ^a Kruskal-Wallis test ^b Pearson chi-square test

Other race include: Asian (n= 11), Native Hawaiian or other Pacific Islander (n=6), American Indian or Alaska Native (n=1), More than 1 race (n=1)

MAC-Myeloablative conditioning; Flu-Fludarabine; Bu-Busulfan; Cy- Cyclophosphamide; HCTCI-hematopoietic cell transplantation comorbidity index; HCT-hematopoietic cell transplantation; DIPSS- dynamic international prognostic scoring system; CMV – cytomegalovirus; TAC- tacrolimus, CSA – cyclosporine; MMF- mycophenolate mofetil; MTX- methotrexate; CY- cyclophosphamide; ATG – antithymocyte globulin; GVHD- graft versus host disease

Supplemental Table S3. Univariable analysis with reduced intensity conditioning (Unadjusted, censored at 24 months)

Outcomes	RIC: Flu/Bu (N = 166)		RIC: Flu/MeI (N = 327)		P Value
	N	Prob (95% CI)	N	Prob (95% CI)	
Non-relapse mortality	164		321		0.21
100-day	Censored 10	4.3 (1.7-7.9)%	6	17.4 (13.5-21.8)%	<0.001
	Event 7		56		
	N at risk 148		261		
1-year	Censored 73	19.9 (14.1-26.5)%	146	27.3 (22.5-32.3)%	0.06
	Event 25		30		
	N at risk 51		86		
2-year	Censored 13	26.8 (20-34.2)%	28	28.7 (23.7-33.9)%	0.67
	Event 9		3		
	N at risk 27		52		
Relapse	164		321		0.08
1-year	Censored 37	48.8 (41-56.6)%	109	41.7 (36.2-47.2)%	0.14
	Event 78		129		
	N at risk 51		86		
2-year	Censored 21	49.6 (41.8-57.4)%	26	44 (38.4-49.7)%	0.26
	Event 1		5		
	N at risk 27		52		
Disease Free-Survival	164		321		0.99
1-year	Censored 5	31.3 (24.3-38.7)%	23	31.1 (26-36.4)%	0.96
	Event 110		215		
	N at risk 49		83		
2-year	Censored 12	23.6 (17.2-30.8)%	23	27.3 (22.2-32.6)%	0.40
	Event 10		8		
	N at risk 27		52		
Overall Survival	166		327		0.43
1-year	Censored 12	68.7 (61.3-75.7)%	45	65.6 (60.2-70.7)%	0.49
	Event 50		109		
	N at risk 104		173		
2-year	Censored 24	56.9 (48.7-64.8)%	60	56.7 (50.8-62.6)%	0.98
	Event 15		18		
	N at risk 65		95		
Acute GVHD II-IV	164		325		0.63
100-day	Censored 9	35.5 (28.3-43)%	42	40.1 (34.8-45.5)%	0.32
	Event 58		130		
	N at risk 98		154		

Outcomes	RIC: Flu/Bu (N = 166)			RIC: Flu/Mel (N = 327)		
		N	Prob (95% CI)	N	Prob (95% CI)	P Value
6 months	Censored	18	43.9 (36.3-51.6)%	14	43.6 (38.2-49)%	0.95
	Event	13		11		
	N at risk	68		130		
1-year	Censored	13	46.7 (38.9-54.5)%	31	45.4 (40-50.9)%	0.79
	Event	4		5		
	N at risk	50		96		
Acute GVHD III-IV		165		326		0.12
6 months	Censored	33	18.5 (12.9-24.9)%	64	22.8 (18.4-27.5)%	0.26
	Event	30		75		
	N at risk	103		190		
1-year	Censored	19	18.5 (12.9-24.9)%	49	23.9 (19.4-28.7)%	0.16
	Event	1		3		
	N at risk	83		141		
2-year	Censored	31	18.5 (12.9-24.9)%	61	23.9 (19.4-28.7)%	0.16
	Event	0		0		
	N at risk	51		74		
Chronic GVHD		165		323		0.15
1-year	Censored	56	44.6 (36.7-52.6)%	139	35.2 (29.8-40.8)%	0.05
	Event	68		104		
	N at risk	42		83		
2-year	Censored	15	50.1 (41.8-58.4)%	32	47.8 (41.7-54)%	0.66
	Event	6		24		
	N at risk	20		24		
GRFS		164		320		0.30
1-year	Censored	5	12.3 (7.6-17.9)%	19	11.6 (8.2-15.6)%	0.84
	Event	140		273		
	N at risk	19		28		
2-year	Censored	5	8.9 (4.8-14.2)%	7	4.7 (2.2-7.9)%	0.12
	Event	4		13		
	N at risk	10		8		

RIC-Reduced intensity conditioning; Flu-Fludarabine; Bu-Busulfan; Mel- Melphalan; GVHD- Graft-versus-host disease; GRFS- GVHD-Free Relapse-Free survival

**Supplemental Table S4. Univariable analysis with myeloablative conditioning
(Unadjusted, censored at 24 months)**

Outcomes	MAC: Flu/Bu (N = 247)		MAC: Bu/Cy (N = 132)		P Value
	N	Prob (95% CI)	N	Prob (95% CI)	
Non-relapse mortality	242		132		0.28
100-day	Censored 12	6.2 (3.5-9.6)%	4	9.1 (4.8-14.6)%	0.32
	Event 15		12		
	N at risk 216		117		
1-year	Censored 102	15.7 (11.3-20.6)%	43	19 (12.8-26.2)%	0.42
	Event 22		13		
	N at risk 92		61		
2-year	Censored 24	16.8 (12.2-21.9)%	3	21.5 (14.8-29)%	0.28
	Event 2		3		
	N at risk 65		54		
Relapse	242		132		0.24
1-year	Censored 63	38.2 (32-44.6)%	29	32.9 (25.1-41.2)%	0.31
	Event 88		43		
	N at risk 92		61		
2-year	Censored 22	40.5 (34.1-47)%	5	33.7 (25.8-42.1)%	0.20
	Event 4		1		
	N at risk 65		54		
Disease-Free Survival	242		132		0.81
1-year	Censored 26	46.2 (39.7-52.6)%	4	48.1 (39.6-56.7)%	0.72
	Event 125		68		
	N at risk 91		60		
2-year	Censored 20	42.7 (36.3-49.3)%	2	44.8 (36.4-53.4)%	0.70
	Event 6		4		
	N at risk 65		54		
Overall Survival	247		132		0.71
1-year	Censored 38	78 (72.5-83.1)%	8	77.8 (70.4-84.5)%	0.96
	Event 52		29		
	N at risk 157		95		
2-year	Censored 38	72.1 (65.9-78)%	12	70.7 (62.4-78.3)%	0.77
	Event 10		8		
	N at risk 109		75		
Acute GVHD II-IV	244		129		<0.001
100-day	Censored 13	34.1 (28.3-40.2)%	7	58.9 (50.3-67.3)%	<0.001
	Event 83		76		
	N at risk 149		47		

Outcomes	MAC: Flu/Bu (N = 247)			MAC: Bu/Cy (N = 132)		
		N	Prob (95% CI)	N	Prob (95% CI)	P Value
6 months	Censored	18	43 (36.8-49.3)%	1	62.8 (54.2-71)%	<0.001
	Event	21		5		
	N at risk	111		41		
1-year	Censored	26	47.5 (41.1-53.9)%	1	62.8 (54.2-71)%	0.004
	Event	9		0		
	N at risk	75		40		
Acute GVHD III-IV		244		127		<0.001
6 months	Censored	39	16.6 (12.1-21.5)%	10	34.6 (26.6-43.2)%	<0.001
	Event	40		44		
	N at risk	168		75		
1-year	Censored	33	19.5 (14.6-24.8)%	8	34.6 (26.6-43.2)%	0.002
	Event	6		0		
	N at risk	127		67		
2-year	Censored		19.5 (14.6-24.8)%		34.6 (26.6-43.2)%	0.002
	Event					
	N at risk	82		53		
Chronic GVHD		242		131		0.29
1-year	Censored	73	46.1 (39.4-52.8)%	30	47.6 (38.9-56.3)%	0.78
	Event	100		61		
	N at risk	70		41		
2-year	Censored	21	53.3 (46.3-60.1)%	9	58.1 (49.1-66.8)%	0.40
	Event	12		11		
	N at risk	36		20		
GRFS		241		127		<0.001
1-year	Censored	14	19.2 (14.3-24.6)%	3	13.4 (8-19.9)%	0.15
	Event	186		109		
	N at risk	41		15		
2-year	Censored	6	14.9 (10.5-20)%	0	8.9 (4.5-14.7)%	0.09
	Event	9		5		
	N at risk	26		10		

MAC-Myeloablative conditioning; Flu-Fludarabine; Bu-Busulfan; Cy- Cyclophosphamide; GVHD- Graft-versus-host disease; GRFS-GVHD-Free Relapse-Free survival

Supplemental Table S5. Multivariable Analyses - reduced intensity conditioning

Overall Survival			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value
Main Effect (<= 6 months)						
RIC: Flu/Bu	166	1.00	Reference			0.009
RIC: Flu/Mel	326	1.80	1.15	2.81	0.009	
Main Effect (> 6 months)						
RIC: Flu/Bu	133	1.00	Reference			0.35
RIC: Flu/Mel	239	0.82	0.53	1.26	0.35	
ATG/alemtuzumab						
No	324	1.00	Reference			0.03
Yes	168	1.39	1.03	1.88	0.03	
<hr/>						
Disease Free Survival			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value
Main Effect (<= 6 months)						
RIC: Flu/Bu	164	1.00	Reference			0.85
RIC: Flu/Mel	320	1.03	0.77	1.38	0.85	
Main Effect (> 6 months)						
RIC: Flu/Bu	92	1.00	Reference			0.76
RIC: Flu/Mel	181	0.95	0.68	1.34	0.76	

Relapse						Overall p-value
Variable	N	HR	95% CI Lower Limit	95% CI Upper Limit	p-value	
Main Effect						0.25
RIC: Flu/Bu	165	1.00	Reference			
RIC: Flu/Mel	320	0.85	0.64	1.12	0.25	
Year of transplant						0.01
2008-2014	116	1.00	Reference			
2015-2019	369	1.53	1.08	2.17	0.01	
Non-Relapse Mortality						
Variable	N	HR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
Main Effect (<=6 months)						0.01
RIC: Flu/Bu	164	1.00	Reference			
RIC: Flu/Mel	320	1.81	1.12	2.91	0.01	
Main Effect (> 6 months)						0.02
RIC: Flu/Bu	92	1.00	Reference			
RIC: Flu/Mel	181	0.46	0.23	0.91	0.02	
Acute GVHD II-IV						
Variable	N	HR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
Main Effect (<=2 months)						0.03
RIC: Flu/Bu	164	1.00	Reference			

RIC: Flu/Mel	324	1.45	1.03	2.03	0.03	
Main Effect (> 2 months)						0.18
RIC: Flu/Bu	111	1.00	Reference			
RIC: Flu/Mel	174	0.71	0.43	1.17	0.18	

Acute GVHD III-IV			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value
Main Effect (<=2 months)						0.004
RIC: Flu/Bu	165	1.00	Reference			
RIC: Flu/Mel	325	2.21	1.28	3.83	0.004	
Main Effect (>2 months)						0.48
RIC: Flu/Bu	143	1.00	Reference			
RIC: Flu/Mel	226	0.89	0.64	1.24	0.48	

Chronic GVHD (adjusted center effect)						Overall p-value
Variable	N	HR	95% CI Lower Limit	95% CI Upper Limit	p-value	
Main Effect						0.55
RIC: Flu/Bu	165	1.00	Reference			
RIC: Flu/Mel	322	0.91	0.67	1.25	0.55	
Donor type						
HLA-identical sibling	139	1.00	Reference			0.03

8/8-matched unrelated donor	309	0.97	0.69	1.35	0.83
7/8-matched unrelated donor	39	1.89	1.15	3.12	0.01

Contrast

8/8-matched unrelated vs 7/8-matched unrelated donor	0.51	0.30	0.88	0.01
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GRFS		95% CI		95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value	
Main Effect						0.32
RIC: Flu/Bu	164	1.00	Reference			
RIC: Flu/Mel	319	1.11	0.90	1.35	0.32	

**RIC- reduced intensity conditioning; Flu/Bu – Fludarabine/busulfan; Flu/Mel- Fludarabine/melphalan; HCT- hematopoietic cell transplantation; ATG – antithymocyte globulin; GVHD- graft versus host disease; GRFS – GVHD-free relapse-free survival

The following factors were considered in the multivariable analysis - patient age, race/ethnicity, disease subtype, dynamic international performance scoring system (DIPSS) score, Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), Karnofsky Performance Scale (KPS), splenic radiation, splenomegaly at HCT, ruxolitinib use pre-transplant, donor-recipient HLA-match, gender match, CMV match, stem cell source, GVHD prophylaxis, use of antithymocyte globulin (ATG)/alemtuzumab, and year of transplant. Significant covariates are shown in table.

Supplemental Table S6. Multivariable Analyses for patients who received myeloablative conditioning

Overall Survival			95% CI		95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value		
Main Effect							0.54
MAC: Flu/Bu	247	1.00	Reference				
MAC: Bu/Cy	132	1.14	0.75	1.71	0.54		
Donor type							<0.001
HLA-identical sibling	132	1.00	Reference				
8/8-matched unrelated	204	1.78	1.09	2.89	0.02		
7/8-matched unrelated	43	3.33	1.83	6.06	<0.001		
Contrast							
8/8-matched unrelated vs 7/8-matched unrelated donor		0.53	0.32	0.89	0.01		
Disease Free Survival			95% CI		95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value		
Main Effect							0.83
MAC: Flu/Bu	238	1.00	Reference				
MAC: Bu/Cy	131	1.03	0.77	1.38	0.83		
Karnofsky score							0.006
90-100	238	1.00	Reference				

< 90	131	1.47	1.11	1.95	0.006	
Ruxolitinib use prior to HCT						0.04
No	170	1.00	Reference			
Yes	199	1.33	1.01	1.77	0.04	
<hr/>						
Relapse			95% CI	95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value	
Main Effect						0.65
MAC: Flu/Bu	238	1.00	Reference			
MAC: Bu/Cy	131	0.92	0.64	1.32	0.65	
Karnofsky score						0.006
90-100	238	1.00	Reference			
< 90	131	1.61	1.14	2.26	0.006	
Ruxolitinib use prior to HCT						0.01
No	170	1.00	Reference			
Yes	199	1.56	1.10	2.21	0.01	
<hr/>						
Non Relapse Mortality			95% CI	95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value	
Main Effect						0.22
MAC: Flu/Bu	242	1.00	Reference			

MAC: Bu/Cy	132	1.36	0.83	2.21	0.22	
Donor type						<0.001
HLA-identical sibling	131	1.00	Reference			
8/8-matched unrelated	201	2.66	1.36	5.18	0.004	
7/8-matched unrelated	42	5.33	2.44	11.61	<0.001	
Contrast						
8/8-matched unrelated vs 7/8-matched unrelated donor		0.50	0.28	0.90	0.02	
<hr/>						
Acute GVHD II-IV			95% CI	95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value	
Main Effect (<=2 months)						<0.001
MAC: Flu/Bu	244	1.00	Reference			
MAC: Bu/Cy	129	2.33	1.67	3.25	<0.001	
Main Effect(> 2 months)						0.69
MAC: Flu/Bu	163	1.00	Reference			
MAC: Bu/Cy	53	0.88	0.46	1.68	0.69	
Donor type						<0.001
HLA-identical sibling	130	1.00	Reference			
8/8-matched unrelated	200	1.45	1.05	1.99	0.02	
7/8-matched unrelated	43	2.53	1.63	3.93	<0.001	

Contrast

8/8-matched unrelated vs 7/8-matched unrelated donor

0.57 0.38 0.86 0.007

Acute GVHD III-IV		95% CI		95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value	
Main Effect						<0.001
MAC: Flu/Bu	244	1.00	Reference			
MAC: Bu/Cy	127	2.31	1.52	3.52	<0.001	
Ruxolitinib use prior to HCT						0.02
No	170	1.00	Reference			
Yes	201	1.67	1.08	2.58	0.02	

Chronic GVHD (adjusted center effect)		95% CI		95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value	
Main Effect						
MAC: Flu/Bu	242	1.00	Reference			0.36
MAC: Bu/Cy	131	1.21	0.80	1.84	0.36	
Ruxolitinib use prior to HCT						
No	172	1.00	Reference			0.02
Yes	201	0.74	0.57	0.96	0.02	

GRFS		95% CI		95% CI		Overall p-value
Variable	N	HR	Lower Limit	Upper Limit	p-value	
Main Effect						<0.001
MAC: Flu/Bu	241	1.00	Reference			
MAC: Bu/Cy	127	1.94	1.49	2.53	<.0001	
Recipient age						0.001
18-49	56	1.00	Reference			
50-59	171	0.74	0.53	1.03	0.07	
>=60	141	1.22	0.85	1.74	0.27	
Donor type						<0.001
HLA-identical sibling	127	1.00	Reference			
8/8-matched unrelated	198	1.31	1.02	1.69	0.03	
7/8-matched unrelated	43	2.41	1.66	3.51	<0.001	
Contrast						
Age 50-59 vs >=60		0.61	0.47	0.79	<0.001	
8/8-matched unrelated vs 7/8-matched unrelated donor		0.54	0.38	0.77	<0.001	

**MAC- myeloablative conditioning; Flu/Bu – Fludarabine/busulfan; Bu/Cy- Busulfan/cyclophosphamide; HCT- hematopoietic cell transplantation; ATG – antithymocyte globulin; GVHD- graft versus host disease; GRFS – GVHD-free relapse-free survival

The following factors were considered in the multivariable analysis - patient age, race/ethnicity, disease subtype, dynamic international performance scoring system (DIPSS) score, Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), Karnofsky Performance Scale (KPS), splenic radiation, splenomegaly at HCT, ruxolitinib use pre-transplant, donor-recipient HLA-match, gender match, CMV match, stem cell source, GVHD prophylaxis, use of antithymocyte globulin (ATG)/alemtuzumab, and year of transplant. Significant covariates are shown in table.

Supplemental Table S7. Multivariable Analyses with RIC – analyzed based on melphalan dose

Overall Survival			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value
Main Effect (<= 6 months)						0.02
RIC: Flu/Bu	166	1.00	Reference			
RIC: Flu/Mel-100	52	2.07	1.08	3.97	0.02	
RIC: Flu/Mel-140	274	1.75	1.11	2.77	0.01	
Main Effect (> 6 months)						0.45
RIC: Flu/Bu	133	1.00	Reference			
RIC: Flu/Mel-100	32	1.12	0.50	2.52	0.78	
RIC: Flu/Mel-140	207	0.78	0.49	1.22	0.27	
ATG/alemtuzumab						0.03
No	324	1.00	Reference			
Yes	168	1.38	1.03	1.88	0.03	
Contrast						
<=6 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		1.18	0.66	2.11	0.56	
>6 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		1.44	0.64	3.21	0.37	
Disease Free Survival			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value

Main Effect (<= 6 months)

RIC: Flu/Bu	164	1.00	Reference			0.87
RIC: Flu/Mel-100	51	1.14	0.70	1.85	0.61	
RIC: Flu/Mel-140	269	1.01	0.75	1.37	0.94	

Main Effect (> 6 months)

RIC: Flu/Bu	92	1.00	Reference			0.91
RIC: Flu/Mel-100	24	1.03	0.55	1.93	0.92	
RIC: Flu/Mel-140	157	0.94	0.66	1.33	0.72	

Contrast

<=6 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		1.12	0.71	1.79	0.62	
>6 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		1.10	0.60	2.01	0.76	

Relapse			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value
Main Effect						0.47
RIC: Flu/Bu	164	1.00	Reference			
RIC: Flu/Mel-100	51	0.76	0.45	1.30	0.32	
RIC: Flu/Mel-140	269	0.86	0.64	1.14	0.30	
Year of transplant						0.01
2008-2014	116	1.00	Reference			
2015-2019	368	1.53	1.08	2.18	0.01	

Contrast						
RIC: Flu/Mel-100 vs RIC: Flu/Mel-140						
		0.89	0.53	1.48		0.66
Non relapse mortality						
			95% CI	95% CI		
			Lower Limit	Upper Limit		
Variable	N	HR			p-value	Overall p-value
Main Effect (<=6 months)						0.03
RIC: Flu/Bu	164	1.00	Reference			
RIC: Flu/Mel-100	51	2.28	1.17	4.47	0.01	
RIC: Flu/Mel-140	269	1.71	1.05	2.80	0.03	
Main Effect (>6 months)						
RIC: Flu/Bu	92	1.00	Reference			0.07
RIC: Flu/Mel-100	24	0.55	0.12	2.37	0.42	
RIC: Flu/Mel-140	157	0.44	0.22	0.91	0.02	
Contrast						
<=6 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140						
		1.33	0.74	2.38		0.33
>6 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140						
		1.23	0.27	5.45		0.78

Acute GVHD II-IV			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value
Main Effect (<= 2 months)						0.10
RIC: Flu/Bu	164	1.00	Reference			
RIC: Flu/Mel-100	52	1.47	0.85	2.54	0.16	
RIC: Flu/Mel-140	272	1.44	1.01	2.04	0.04	
Main Effect (> 2 months)						0.34
RIC: Flu/Bu	111	1.00	Reference			
RIC: Flu/Mel-100	29	0.91	0.37	2.19	0.83	
RIC: Flu/Mel-140	145	0.67	0.39	1.14	0.14	
Contrast						
<=2 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		1.02	0.61	1.69	0.92	
>2 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		1.34	0.55	3.26	0.51	
Acute GVHD III-IV			95% CI	95% CI		
Variable	N	HR	Lower Limit	Upper Limit	p-value	Overall p-value
Main Effect (<= 2						0.005

months)

RIC: Flu/Bu	165	1.00	Reference		
RIC: Flu/Mel-100	52	1.31	0.51	3.35	0.57
RIC: Flu/Mel-140	273	2.38	1.36	4.15	0.002

Main Effect (>2 months)

0.42

RIC: Flu/Bu	143	1.00	Reference		
RIC: Flu/Mel-100	41	0.47	0.10	2.08	0.32
RIC: Flu/Mel-140	185	0.67	0.32	1.39	0.28

Contrast

<=2 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140

0.55 0.23 1.27 0.16

>2 mon: RIC: Flu/Mel-100 vs RIC: Flu/Mel-140

0.70 0.16 3.11 0.64

Chronic GVHD (adjusted center effect)

Variable	N	HR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p-value
Main Effect						0.73
RIC: Flu/Bu	165	1.00	Reference			
RIC: Flu/Mel-100	52	0.80	0.44	1.42	0.45	
RIC: Flu/Mel-140	270	0.92	0.67	1.27	0.64	

Donor type						0.03
HLA-identical sibling	139	1.00	Reference			
8/8-matched unrelated	309	0.97	0.70	1.34		0.86
7/8-matched unrelated	39	1.92	1.17	3.16		0.009

Contrast

8/8-matched unrelated vs 7/8-matched unrelated		0.50	0.29	0.87		0.01
RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		0.86	0.50	1.48		0.59

GRFS

Variable	N	HR	95% CI Lower Limit	95% CI Upper Limit	p-value	Overall p- value
Main Effect						0.60
RIC: Flu/Bu	164	1.00	Reference			
RIC: Flu/Mel-100	51	1.07	0.76	1.52		0.67
RIC: Flu/Mel-140	268	1.11	0.90	1.36		0.32

Contrast

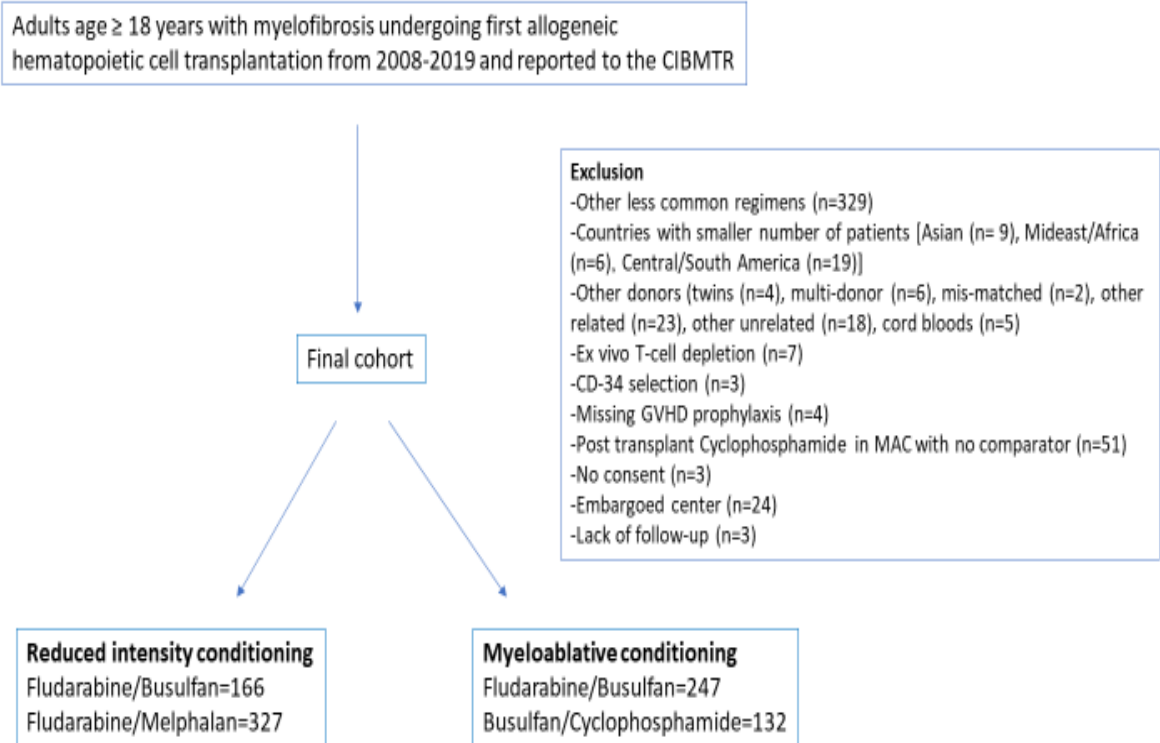
RIC: Flu/Mel-100 vs RIC: Flu/Mel-140		0.97	0.69	1.35		0.85
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*RIC- reduced intensity conditioning; Flu/Bu – Fludarabine/busulfan; Flu/Mel- Fludarabine/melphalan; HCT- hematopoietic cell transplantation; ATG – antithymocyte globulin; GVHD- graft versus host disease; GRFS – GVHD-free relapse-free survival

The following factors were considered in the multivariable analysis - patient age, race/ethnicity, disease subtype, dynamic international performance scoring system (DIPSS) score, Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), Karnofsky Performance Scale (KPS), splenic radiation, splenomegaly at HCT, ruxolitinib use pre-transplant, donor-recipient HLA-match, gender match, CMV match, stem cell source, GVHD prophylaxis, use of antithymocyte globulin (ATG)/alemtuzumab, and year of transplant. Significant covariates are shown in table.

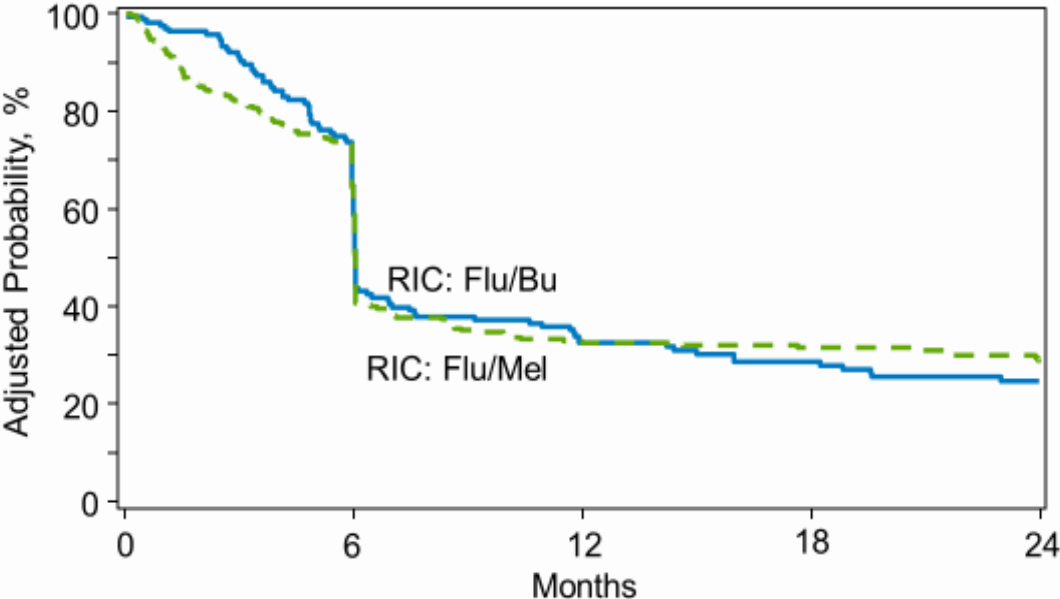
Supplemental Figure S1- Consort diagram

Cohort selection



Supplemental Figure S2 – Disease free survival with reduced intensity conditioning

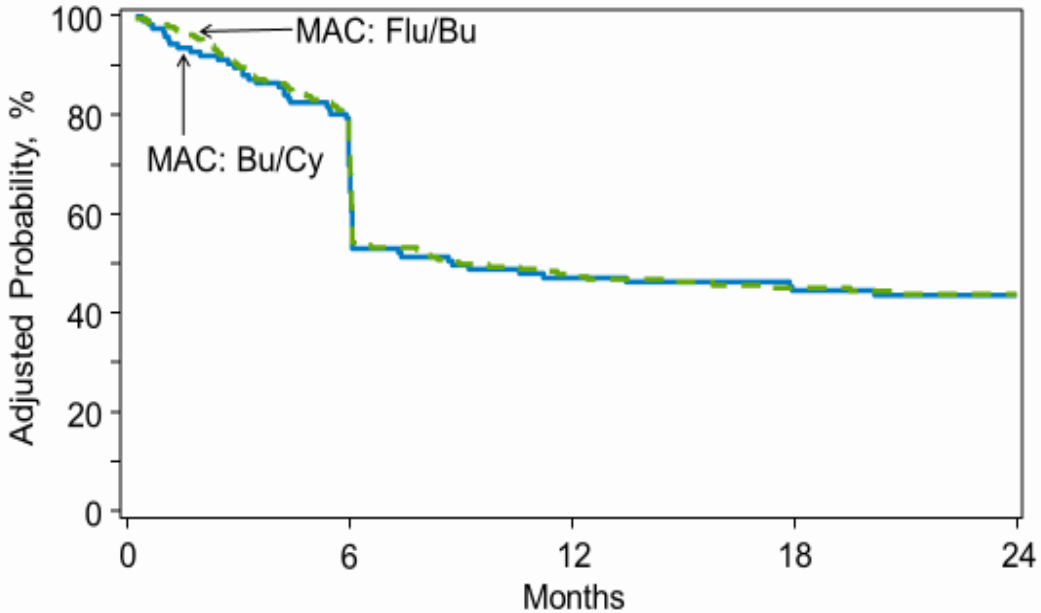
Disease-Free Survival, RIC



N at Risk	0	6	12	18	24
RIC: Flu/Bu	164	92	49	36	27
RIC: Flu/Mel	321	181	83	61	52

Supplemental Figure S3 – Disease free survival with myeloablative conditioning

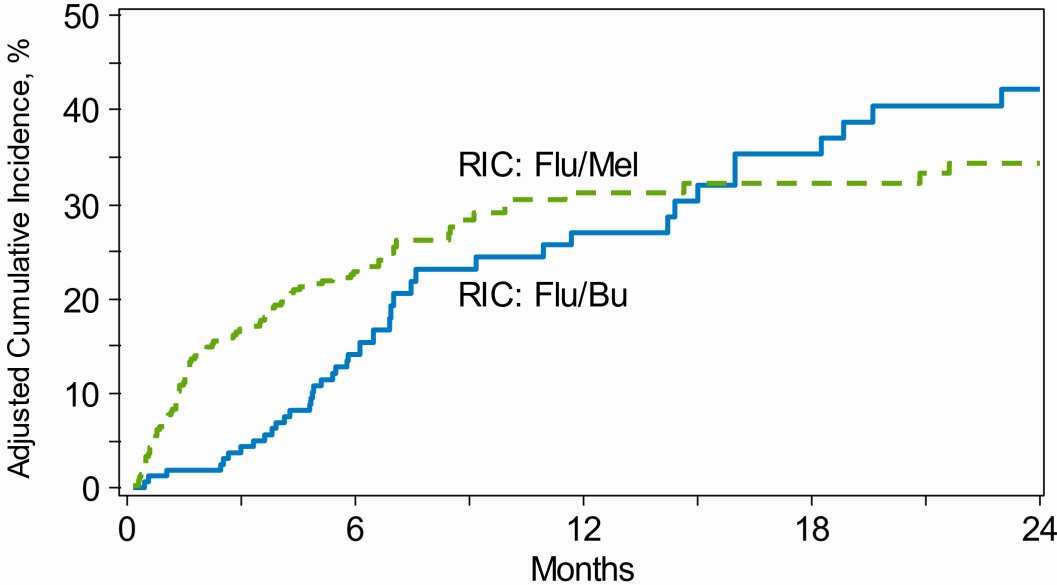
Disease-Free Survival, MAC



N at Risk	0	6	12	18	24
MAC: Flu/Bu	242	154	91	76	65
MAC: Bu/Cy	132	85	60	55	54

Supplemental Figure S4 – Non-relapse mortality with reduced intensity conditioning

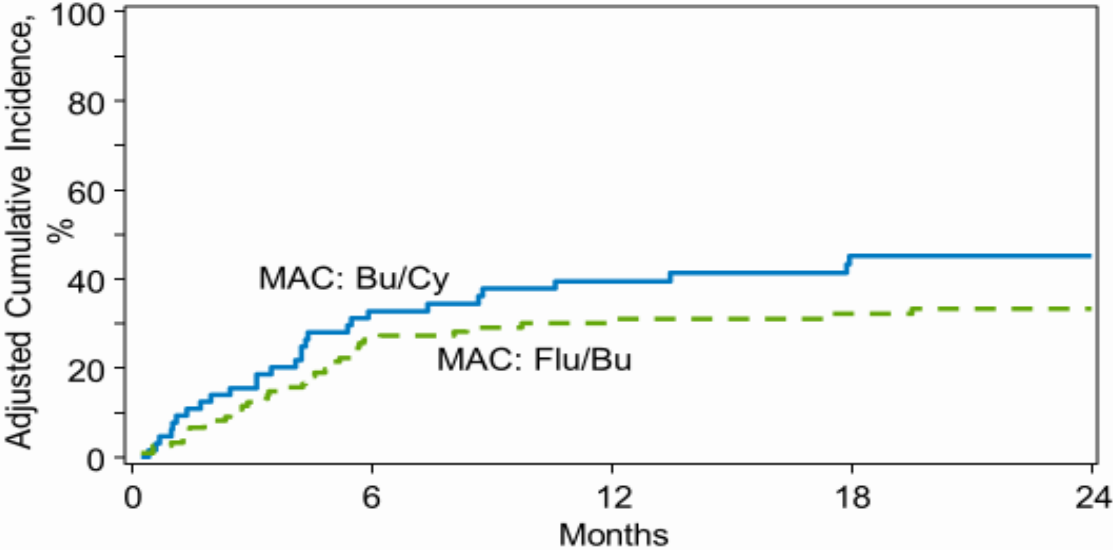
Non-Relapse Mortality for RIC



N at Risk	0	6	12	18	24
RIC: Flu/Bu	164	102	51	38	27
RIC: Flu/Mel	321	200	86	62	52

Supplemental Figure S5 – Non-relapse mortality with myeloablative conditioning

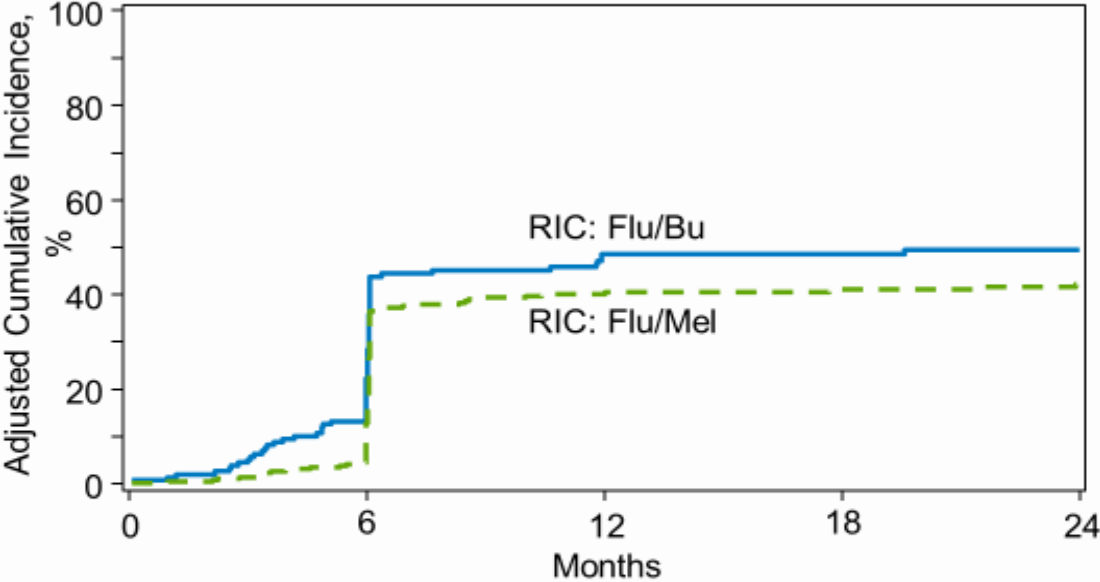
Non-Relapse Mortality, MAC



N at Risk	0	6	12	18	24
MAC: Flu/Bu	242	168	92	77	65
MAC: Bu/Cy	132	92	61	56	54

Supplemental Figure S6 – Relapse with reduced intensity conditioning

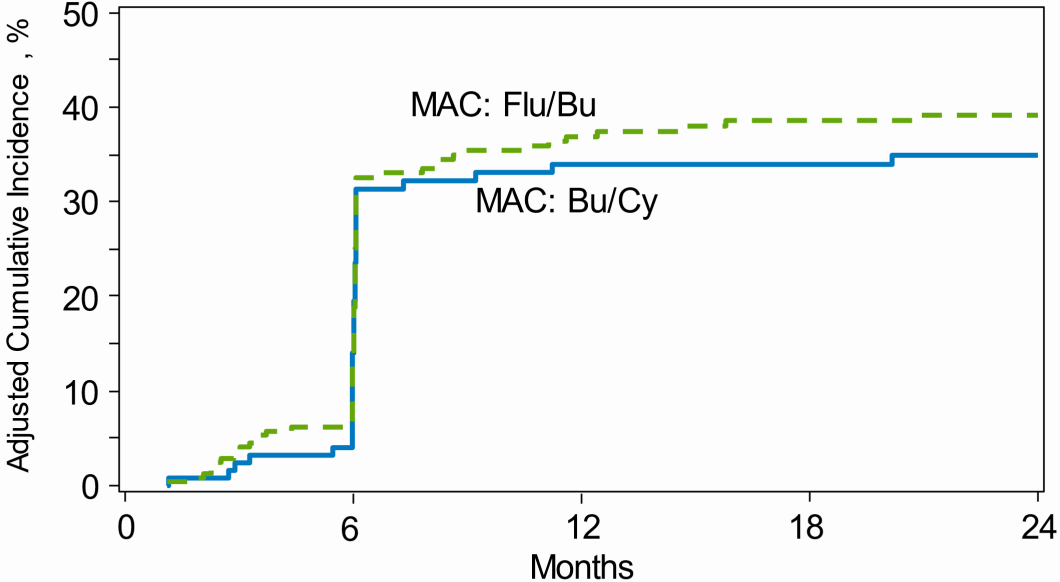
Relapse, RIC



N at Risk	0	6	12	18	24
RIC: Flu/Bu	164	102	51	38	27
RIC: Flu/Mel	321	200	86	62	52

Supplemental Figure S7 – Relapse with myeloablative conditioning

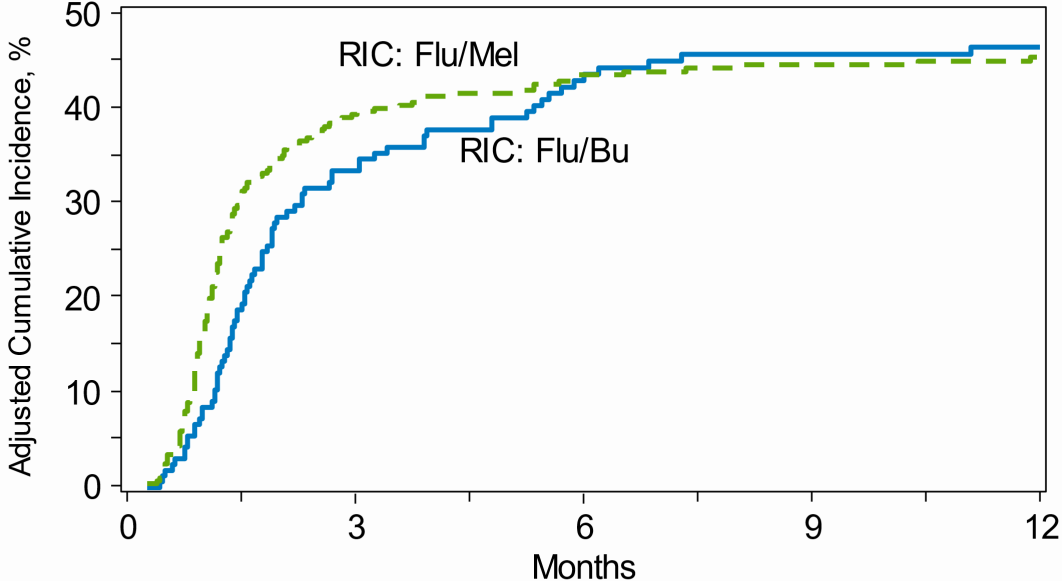
Relapse, MAC



N at Risk	0	6	12	18	24
MAC: Flu/Bu	242	168	92	77	65
MAC: Bu/Cy	132	92	61	56	54

Supplemental Figure S8 – Acute GVHD grade II-IV with reduced intensity conditioning

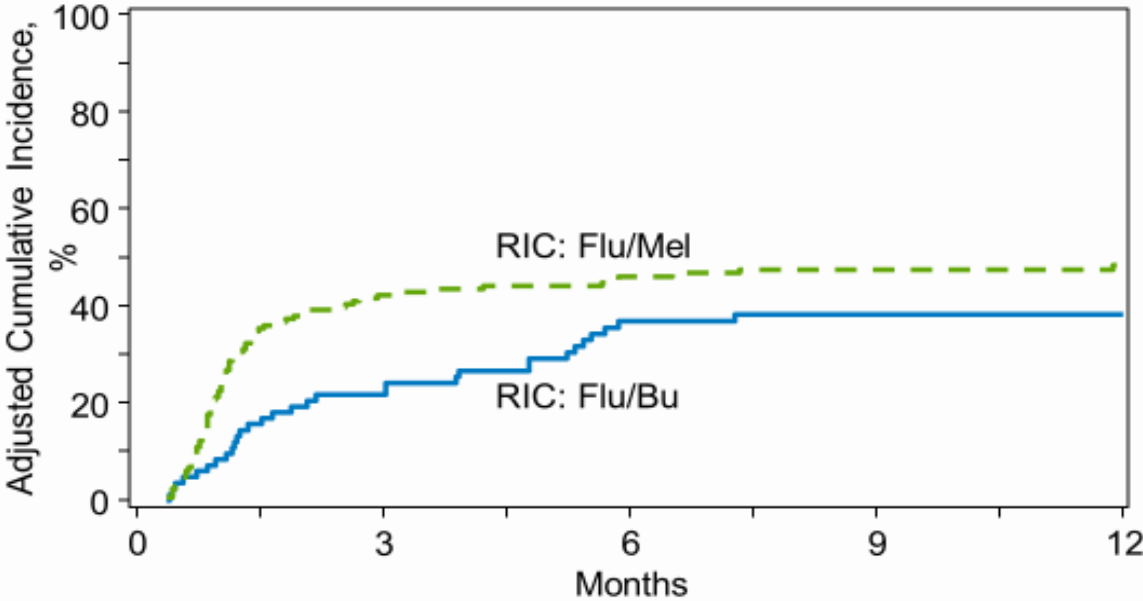
Acute GVHD, Grades II -IV for RIC



N at Risk	0	3	6	9	12
RIC: Flu/Bu	164	98	68	55	50
RIC: Flu/Mel	325	154	130	111	96

Supplemental Figure S9 – Acute GVHD grade III-IV with reduced intensity conditioning

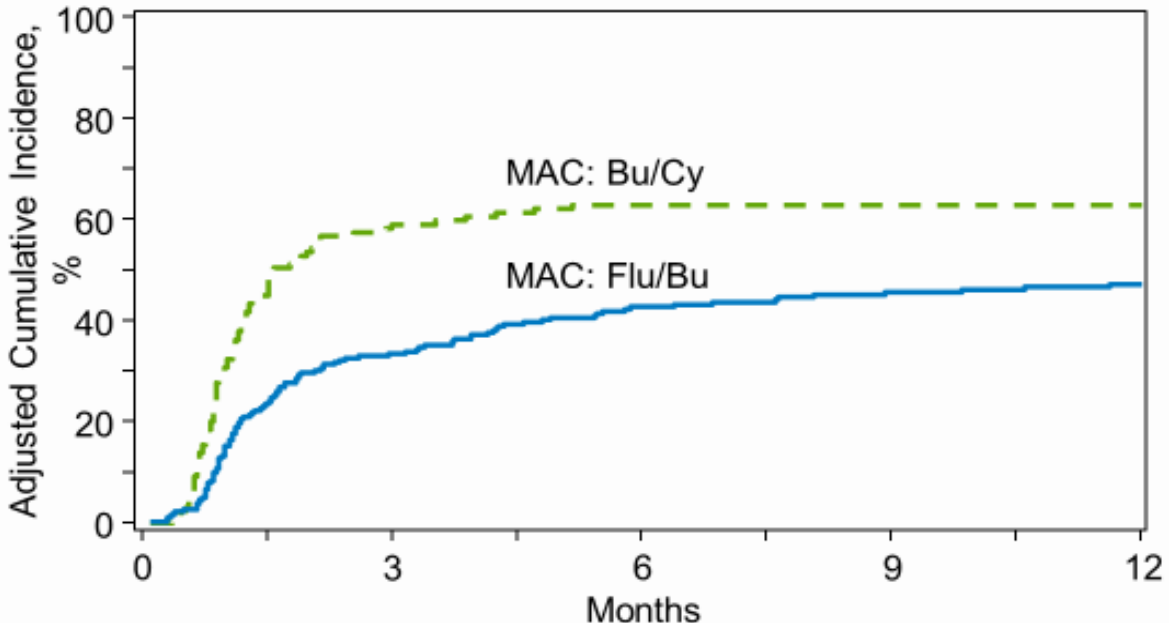
Acute GVHD, Grades III-IV for RIC



N at Risk	0	3	6	9	12
RIC: Flu/Bu	165	135	103	89	83
RIC: Flu/Mel	326	215	190	161	141

Supplemental Figure S10 – Acute GVHD grade II-IV with myeloablative conditioning

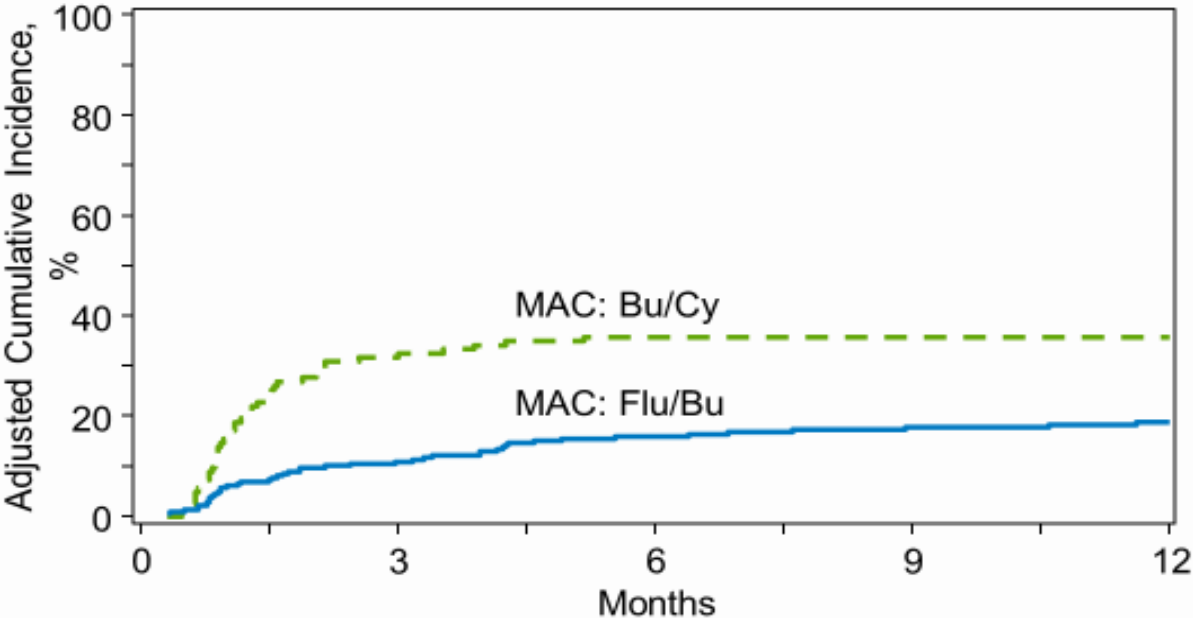
Acute GVHD, Grades II-IV for MAC



N at Risk	0	3	6	9	12
MAC: Flu/Bu	244	149	111	91	75
MAC: Bu/Cy	129	47	41	40	40

Supplemental Figure S11 – Acute GVHD grade III-IV with myeloablative conditioning

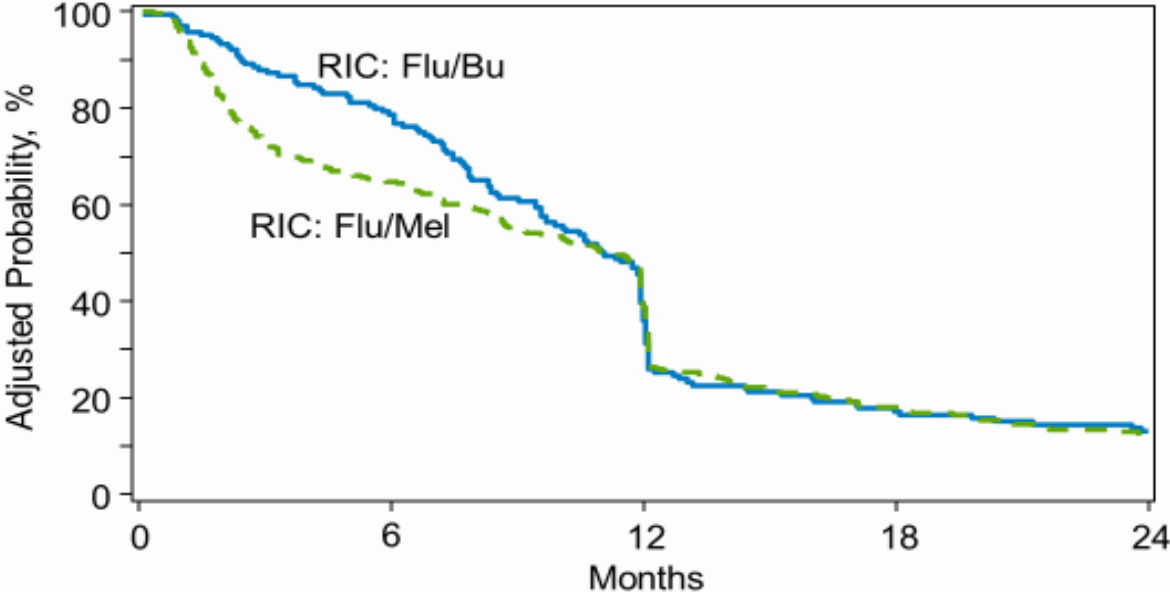
Acute GVHD, Grades III-IV for MAC



N at Risk	0	3	6	9	12
MAC: Flu/Bu	244	199	168	147	127
MAC: Bu/Cy	127	81	75	70	67

Supplemental Figure S12 – GVHD-free Relapse-free Survival with reduced intensity conditioning

GVHD- and Relapse-Free Survival, RIC



N at Risk	0	6	12	18	24
RIC: Flu/Bu	164	56	19	13	10
RIC: Flu/Mel	321	115	28	11	8