

# Mycophenolate mofetil is associated with inferior overall survival in cytomegalovirus-seropositive patients with acute myeloid leukemia undergoing hematopoietic cell transplantation

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**Supplemental Table S1: Multivariate analysis: CNI cohort**

	Overall Survival		Non-relapse mortality		Relapse		Chronic GVHD	
<b>AML</b>	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Main effect								
MTX/CMV-	1.0		1.0		1.0		1.0	
MTX/CMV+	1.2 (0.9-1.4)	0.7	1.2 (0.9-1.6)	0.8	0.9 (0.8-1.2)	0.9	0.9 (0.7-1.1)	0.9
MMF/CMV-	0.9 (0.7-1.3)	0.9	1.4 (0.9-2.1)	0.7	0.8 (0.5-1.0)	0.1	1.4 (1.05-1.8)	0.2
MMF/CMV+	1.8 (1.4-2.3)	<0.001	1.9 (1.3-2.6)	0.002	1.2 (0.9-1.6)	0.1	0.9 (0.7-1.2)	0.9
Patient age/HCT-CI								
< 60 years/ <3	1.0		1.0				1.0	
>60 years/ <3	1.3 (1.03-1.6)	0.02	1.4 (0.9-1.9)	0.06	-	-	1.04 (0.8-1.3)	0.7
< 60 years/ ≥3	1.2 (0.9-1.5)	0.1	1.2 (0.8-1.6)	0.3	-	-	1.03 (0.9-1.2)	0.7
>60 years/ ≥3	1.9 (1.5-2.3)	<0.001	1.8 (1.3-2.4)	<0.001	-	-	0.7 (0.5-0.8)	<0.001
Advanced disease	2.2 (1.9-2.6)	<0.001	1.4 (1.1-1.8)	0.004	2.7 (1.8-3.9)	<0.001	0.7 (0.5-0.8)	<0.001
Donor CMV+							1.2 (1.1-1.4)	0.004
	Overall Survival		Non-relapse mortality		Relapse		Chronic GVHD	
<b>ALL</b>	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Main effect								
MTX/CMV-	1.0		1.0		1.0		1.0	
MTX/CMV+	0.9 (0.7-1.3)	0.9	1.5 (0.8-2.8)	0.9	0.9 (0.5-1.3)	0.9	1.03 (0.7-1.4)	0.9
MMF/CMV-	0.8 (0.4-1.4)	0.9	1.02 (0.5-2.1)	0.9	0.7 (0.3-1.7)	0.9	2.1 (1.3-3.3)	0.01
MMF/CMV+	1.2 (0.7-1.9)	0.9	0.9 (0.6-1.4)	0.9	0.8 (0.4-1.6)	0.9	1.7 (1.04-2.8)	0.2
In vivo depletion	-	-	-	-	-	-	0.7 (0.5-0.9)	0.02
Donor age >35 years	1.5 (1.1-2)	0.004	1.6 (1.1-2.4)	0.01	-	-		
HCT-CI ≥3	1.4 (1.1-1.8)	0.02	-	-	-	-	0.7 (0.5-0.9)	0.02
Intermediate/advanced disease	1.9 (1.4-2.5)	<0.001	-	-	2.9 (1.9-4.2)	<0.001	0.7 (0.5-0.9)	0.04
Female-to-male	-	-	-	-	-	-	1.5 (0.9-2.1)	0.05
Donor/recipient CMV (+/-)	-	-	-	-	0.3 (0.1-0.9)	0.04	-	-
	Overall Survival		Non-relapse mortality		Relapse		Chronic GVHD	
<b>MDS</b>	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	
Main effect								
MTX/CMV-	1.0		1.0*		1.0		1.0	

MTX/CMV+	1.2 (0.99-1.5)	0.3	1.6 (1.1-2.2)	0.03	0.9 (0.8-1.3)	0.9	1.01 (0.8-1.2)	0.9
MMF/CMV-	1.1 (0.8-1.5)	0.9	1.6 (0.9-2.6)	0.2	0.8 (0.5-1.2)	0.9	1.6 (1.2-2.1)	0.01
MMF/CMV+	1.3 (1.0-1.7)	0.2	1.6 (1.05-2.4)	0.1	1.01 (0.7-1.5)	0.9	1.4 (1.1-1.9)	0.1
In vivo T-cell depletion	-	-	-	-	1.3 (0.9-1.6)	0.05	0.7 (0.6-0.9)	0.001
Myeloablative conditioning	-	-	-	-	0.7 (0.5-0.9)	0.006	-	-
Donor age >35 years	1.3 (1.1-1.6)	0.004	1.6 (1.2-2.2)	0.001	-	-	-	-
Age >60 years	1.2 (1.05-1.5)	0.01	-	-	-	-	-	-
HCT-CI $\geq$ 3	1.4 (1.2-1.7)	<0.001	-	-	-	-	-	-
Advanced disease	-	-	-	-	1.6 (1.1-2.3)	0.02	0.8 (0.6-0.9)	0.03

\* in patients with HCT-CI  $\geq$ 3. Among those with HCT-CI 0-2: MTX/CMV- [reference], MTX/CMV+ [HR 0.9 (0.6-1.3), p=0.5], MMF/CMV- [HR 0.9 (0.4-1.7), p=0.7], MMF/CMV+ [HR 1.6 (0.9-2.6), p=0.09]

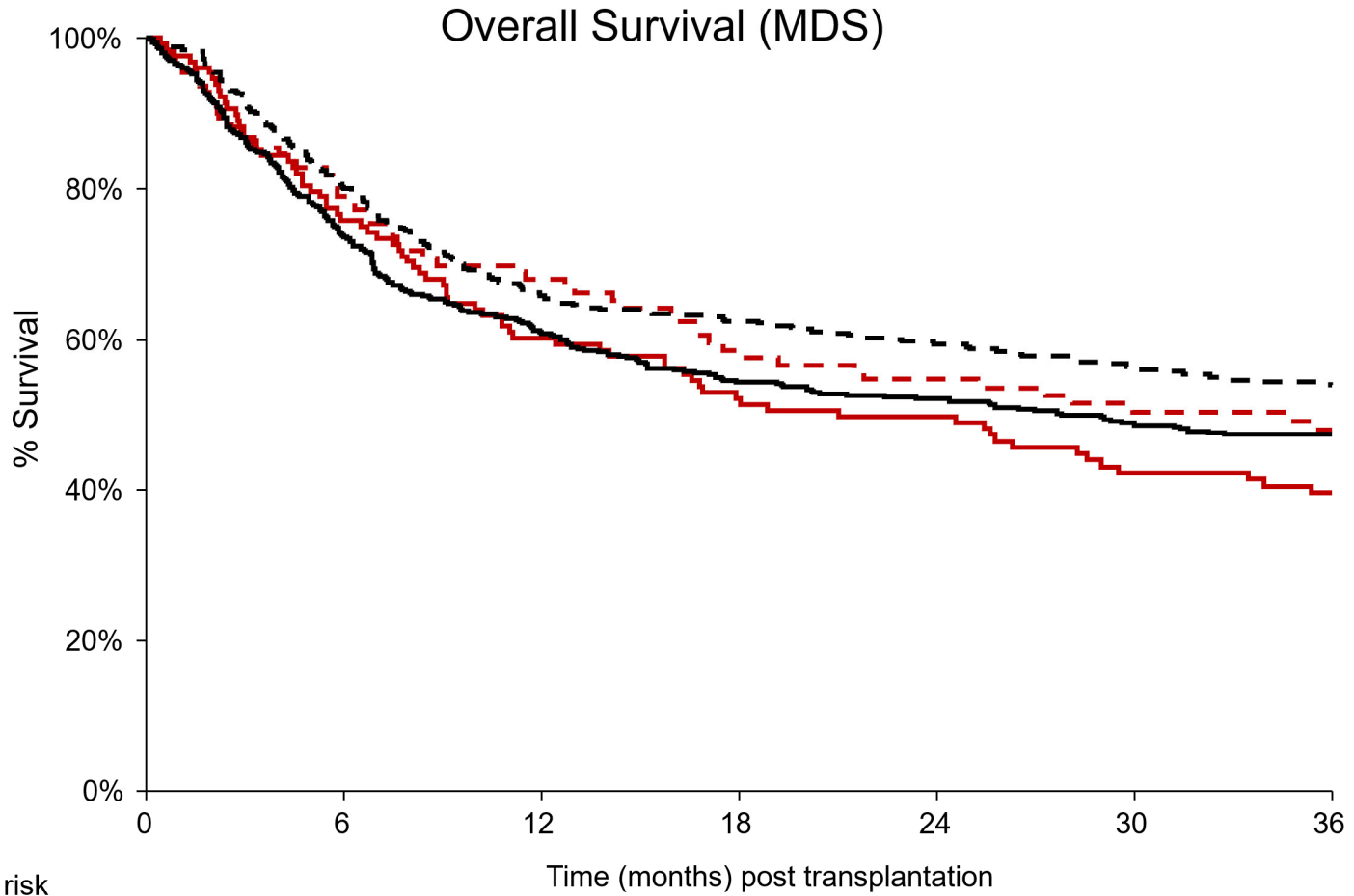
Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CI, confidence interval; CMV, cytomegalovirus; GVHD, graft-versus-host disease; HCT-CI, hematopoietic cell transplantation comorbidity index; HR, Hazard ratio; MDS, myelodysplastic neoplasms; MMF, Mycophenolate Mofetil; MTX, Methotrexate; NRM, non-relapse mortality; OS, overall survival.

**Supplemental Table S2: Baseline Characteristics: PTCy cohort**

	<b>Overall N=242 (%)</b>	<b>MMF/ CMV+ N=150 (%)</b>	<b>MMF/ CMV- N=92 (%)</b>
<b>Recipient age, median (range)</b>	62 (18-80)	62 (25-80)	62 (18-75)
≤40 years	27 (11)	14 (9)	13 (14)
41-50 years	23 (9)	13 (9)	10 (11)
51-60 years	44 (18)	29 (19)	15 (16)
>60 years	148 (61)	94 (63)	54 (59)
<b>Disease</b>			
AML	136 (56)	90 (60)	46 (50)
ALL	42 (17)	32 (21)	10 (11)
MDS	28 (19)	28 (19)	36 (39)
<b>Conditioning intensity</b>			
MAC	85 (35)	52 (35)	33 (36)
RIC/ NMA	157 (65)	98 (65)	59 (64)
<b>Recipient gender</b>			
Male	134 (55)	79 (53)	55 (60)
Female	108 (45)	71 (47)	37 (40)
<b>Disease Risk Index</b>			
Low/intermediate	190 (78)	120 (80)	70 (76)
High/ very high	51 (21)	29 (19)	22 (24)
Missing	1 (0.4)	1 (1)	0
<b>HCT-CI</b>			
0-2	109 (45)	62 (41)	47 (51)
≥3	133 (55)	88 (59)	45 (49)
<b>Donor age</b>			
>35 years	53 (22)	30 (20)	23 (25)
Missing	1	0	1
<b>Follow-up among survivors, in months, median (IQR)</b>	12.7 (12, 34.5)	13 (12, 34.7)	12.6 (12, 32)

*Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CMV, cytomegalovirus; HCT-CI, Hematopoietic Cell Transplantation-specific Comorbidity Index; IQR, interquartile range; MAC, Myeloablative conditioning; MDS, myelodysplastic neoplasms; MMF, Mycophenolate Mofetil; MTX, Methotrexate; NMA, Non-myeloablative Conditioning; PTCy, Post-transplant cyclophosphamide; RIC, Reduced-intensity Conditioning.*

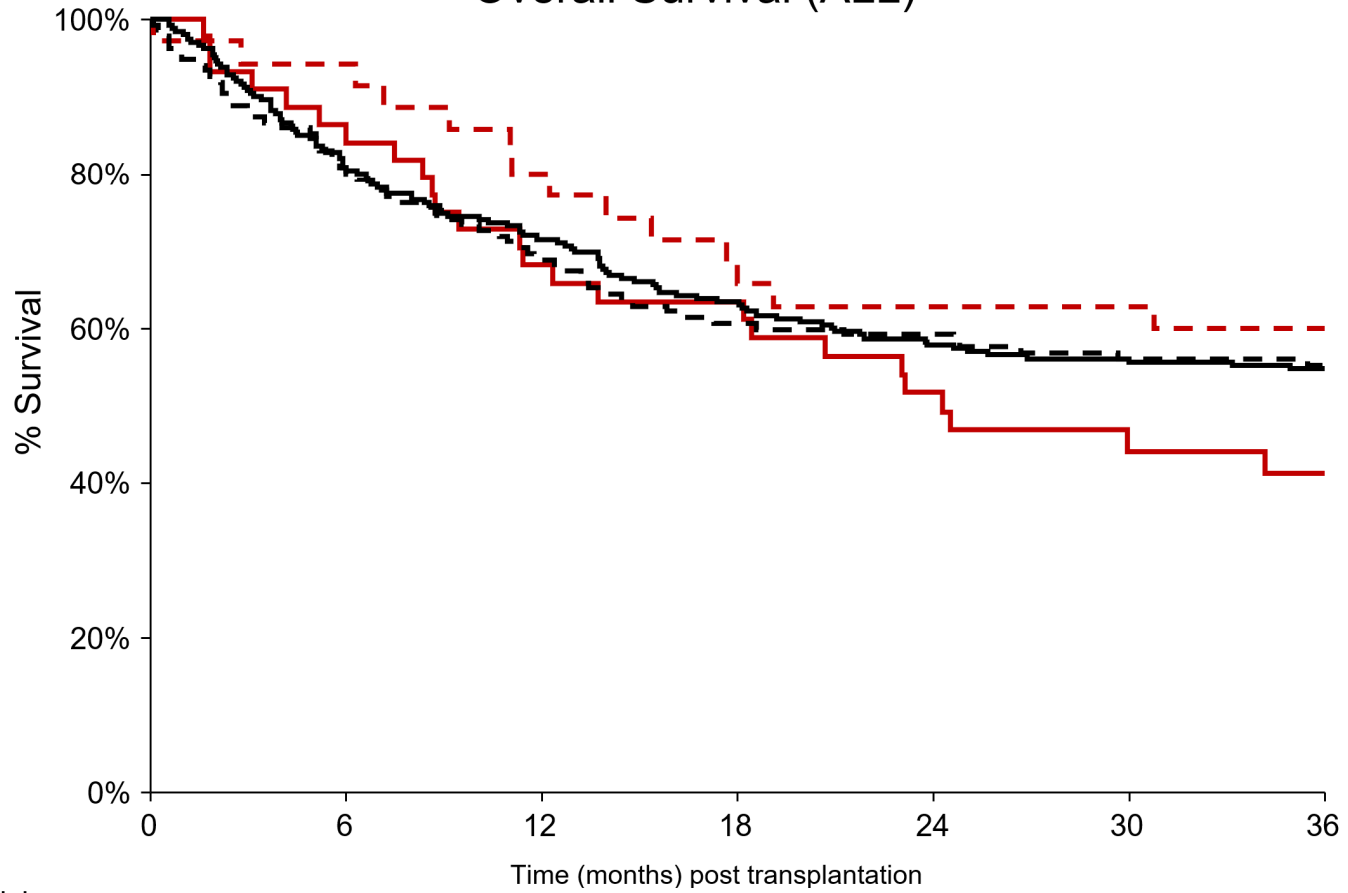
Supplemental Figure 1A



Number at risk		Time (months) post transplantation							
		0	6	12	18	24	30	36	
- - ·	MTX/ CMV-	390	313	251	231	199	167	146	
—	MTX/ CMV+	452	329	268	237	214	184	153	
- - ·	MMF/ CMV-	110	86	74	61	55	46	39	
—	MMF/ CMV+	128	97	77	66	62	49	38	

Supplemental Figure 1B

Overall Survival (ALL)



Number at risk

- - · MTX/ CMV-	135	109	92	81	76	71	60
— MTX/ CMV+	239	192	169	148	134	127	110
- - · MMF/ CMV-	35	33	28	23	22	22	20
— MMF/ CMV+	44	38	29	27	21	16	14

## Figure Legends

**Supplemental Figure 1:** Overall survival in the methotrexate (MTX)/CMV seronegative (-) group (dotted black), MTX/CMV seropositive (+) group (solid black), mycophenolate mofetil (MMF)/CMV seronegative (-) group (dotted maroon) and MMF/CMV seronegative (+) group (solid maroon) among patients with myelodysplastic neoplasm (A), and among patients with acute lymphoblastic leukemia (B).