SUPPLEMENTAL APPENDIX

Table of Contents 1

Table S1: Intensive induction therapies

Cohort	Regimen	N	Total
ALLIANCE/CALGB 50403	Augmented-dose-R-CHOP/methotrexate followed by HD-cytarabine (with stem cell mobilization)	127	127
MCL-RCS	R-hyperCVAD	168	305
	R-M-CHOP	71	
	R-maxi-CHOP alternating with R-HD-cytarabine	20	
	R-CHOP alternating with R-DHAP	34	
	BR alternating with R-HD-cytarabine	6	
	R-DHAP	6	
MER	R-HD-cytarabine based regimens	23	45
	R-hyperCVAD	22	

Table S2: PFS UVA

Covariate	N	HR (95% CI)	p-value
Time to first treatment			
15-60 days	797	Referent	
0-14 days	300	1.69 (1.43-2.00)	**<.001**
Age at diagnosis, continuous	1094	1.02 (1.01-1.03)	**<.001**
Sex			
Female	256	Referent	
Male	840	1.27 (1.04-1.55)	**0.02**
Race			
White	970	Referent	
Black	40	0.99 (0.62-1.59)	0.98
Others	40	1.17 (0.74-1.86)	0.49
ECOG PS			
0	601	Referent	
1	335	1.48 (1.24-1.76)	**<.001**
≥2	67	2.20 (1.62-2.99)	**<.001**
Ann Arbor Stage			
1-3	152	Referent	
4	934	1.39 (1.10-1.76)	**0.006**
LDH			
Normal	514	Referent	
Elevated	332	1.63 (1.35-1.96)	**<.001**
BM involvement			
No	165	Referent	
Yes	802	1.51 (1.19-1.92)	**<.001**
B symptoms			
No	738	Referent	
Yes	309	1.31 (1.09-1.57)	**0.003**
MIPI			
<5.7	339	Referent	
≥5.7 <6.2	220	1.48 (1.17-1.86)	**<.001**
≥6.2	228	2.06 (1.64-2.58)	**<.001**
Intensive induction therapy			
No	617	Referent	
Yes	477	0.63 (0.54-0.75)	**<.001**

Table S3: OS UVA

Covariate	N	HR (95% CI)	p-value
Time to first treatment			
15-60 days	797	Referent	
0-14 days	300	1.66 (1.34-2.06)	**<.001**
Age at diagnosis, continuous	1094	1.04 (1.03-1.05)	**<.001**
Sex			
Female	256	Referent	
Male	840	1.32 (1.02-1.72)	**0.04**
Race			
White	970	Referent	
Black	40	0.82 (0.41-1.66)	0.58
Others	40	0.88 (0.45-1.71)	0.71
ECOG PS			
0	601	Referent	
1	335	1.47 (1.16-1.85)	**0.001**
≥2	67	3.16 (2.24-4.45)	**<.001**
Ann Arbor Stage			
1-3	152	Referent	
4	934	1.64 (1.19-2.27)	**0.003**
LDH			
Normal	514	Referent	
Elevated	332	2.05 (1.62-2.59)	**<.001**
BM involvement			
No	165	Referent	
Yes	802	1.79 (1.29-2.47)	**<.001**
B symptoms			
No	738	Referent	
Yes	309	1.41 (1.13-1.77)	**0.003**
MIPI			
<5.7	339	Referent	
≥5.7 <6.2	220	1.45 (1.06-1.97)	**0.02**
≥6.2	228	2.88 (2.17-3.82)	**<.001**
Intensive induction therapy			
No	617	Referent	
Yes	477	0.59 (0.47-0.74)	**<.001**

Table S4: TTT as a continuous variable: PFS MVA

Covariate	HR (95% CI)	p-value
Time to first treatment (per week)	0.86 (0.82-0.91)	**<.001**
MIPI		
<5.7	Referent	
≥5.7 <6.2	1.30 (1.02-1.65)	**0.03**
≥6.2	1.64 (1.29-2.08)	**<.001**
Intensive induction therapy		
No	Referent	
Yes	0.71 (0.58-0.87)	**0.001**

Table S5: TTT as a continuous variable: OS MVA

Covariate	HR (95% CI)	p-value
Time to first treatment (per week)	0.91 (0.85-0.98)	**0.009**
MIPI		
<5.7	Referent	
≥5.7 <6.2	1.31 (0.95-1.80)	0.10
≥6.2	2.47 (1.83-3.31)	**<.001**
Intensive induction therapy		
No	Referent	
Yes	0.74 (0.57-0.961.20)	**0.02**

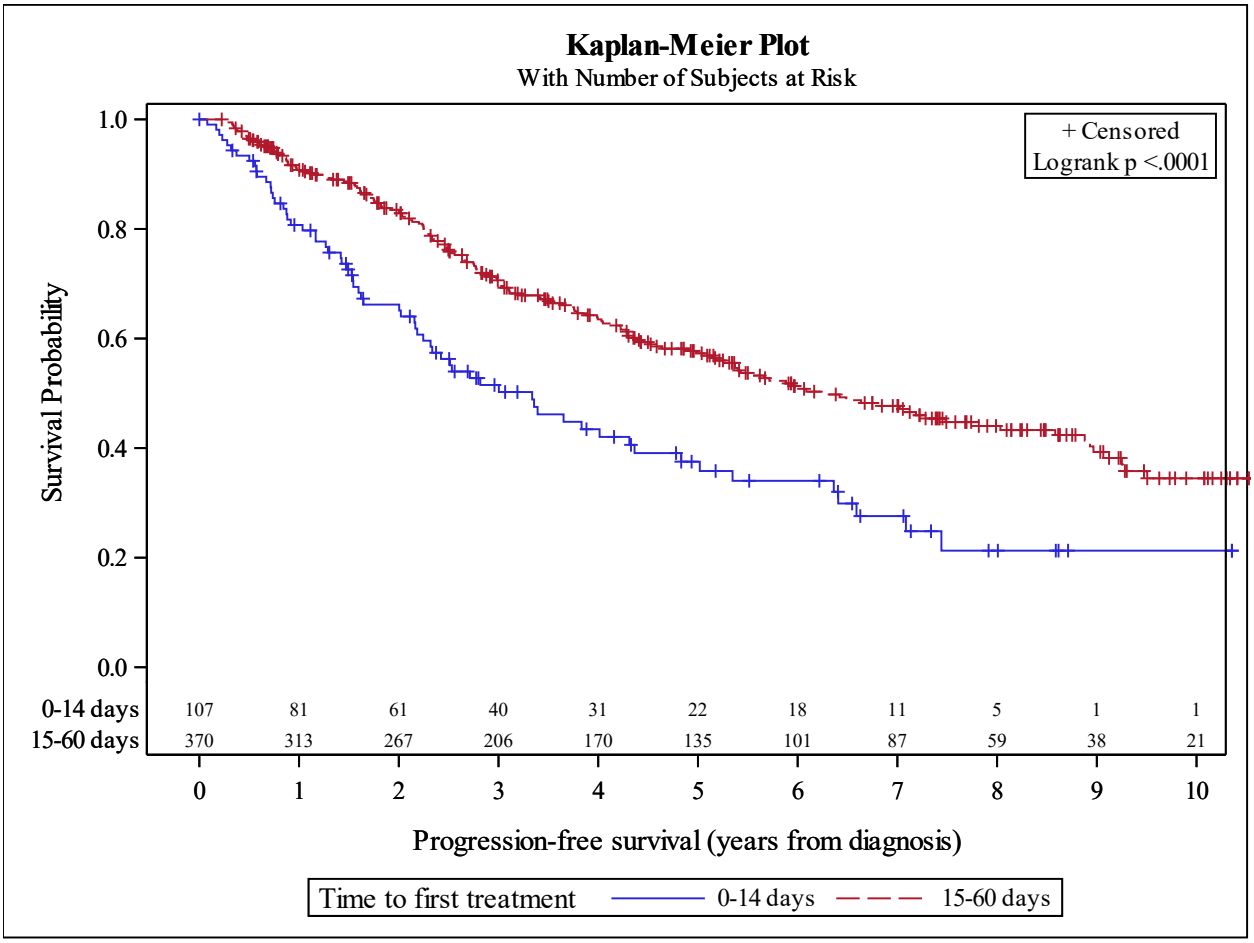
Table S6: Association of TTT with PFS (MVA) after excluding ALLIANCE patient cohort

Covariate	HR (95% CI)	p-value
Time to first treatment		
15-60 days	Referent	
0-14 days	1.44 (1.13-1.82)	**0.003**
Sex		
Female	Referent	
Male	1.42 (1.07-1.89)	**0.01**
Ann Arbor Stage		
1-3	Referent	
4	0.89 (0.54-1.45)	0.63
BM involvement		
No	Referent	
Yes	1.36 (0.86-2.16)	0.19
B symptoms		
No	Referent	
Yes	1.14 (0.88-1.48)	0.31
MIPI		
<5.7	Referent	
≥5.7 <6.2	1.21 (0.91-1.60)	0.19
≥6.2	1.75 (1.31-2.32)	**<.001**
Intensive induction therapy		
No	Referent	
Yes	0.68 (0.53-0.88)	**0.003**

Table S7: Association of TTT and OS (MVA) after excluding ALLIANCE patient cohort

Covariate	HR (95% CI)	p-value
Time to first treatment		
15-60 days	Referent	
0-14 days	1.62 (1.21-2.16)	**0.001**
Sex		
Female	Referent	
Male	1.61 (1.12-2.33)	**0.01**
Ann Arbor Stage		
1-3	Referent	
4	0.87 (0.43-1.76)	0.70
BM involvement		
No	Referent	
Yes	1.36 (0.70-2.67)	0.36
B symptoms		
No	Referent	
Yes	1.01 (0.73-1.41)	0.94
MIPI		
<5.7	Referent	
≥5.7 <6.2	1.43 (0.96-2.11)	0.08
≥6.2	3.27 (2.24-4.77)	**<.001**
Intensive induction therapy		
No	Referent	
Yes	0.55 (0.39-0.79)	**0.001**

Figure S1: PFS between short DTI and long DTI among the recipients of intensive induction therapy



Time to first treatment	No. of Subject	Event	Censored	Median Survival (95% CI)	Time to first treatment	2 Yr Survival	5 Yr Survival
0-14 days	107	64 (60%)	43 (40%)	3.3 (2.2, 4.4)	0-14 days	66.2% (56.0%, 74.6%)	37.5% (27.2%, 47.9%)
15-60 days	370	171 (46%)	199 (54%)	6.3 (5.3, 8)	15-60 days	83.5% (79.1%, 87.0%)	57.3% (51.5%, 62.7%)

Figure S2: Adjusted PFS

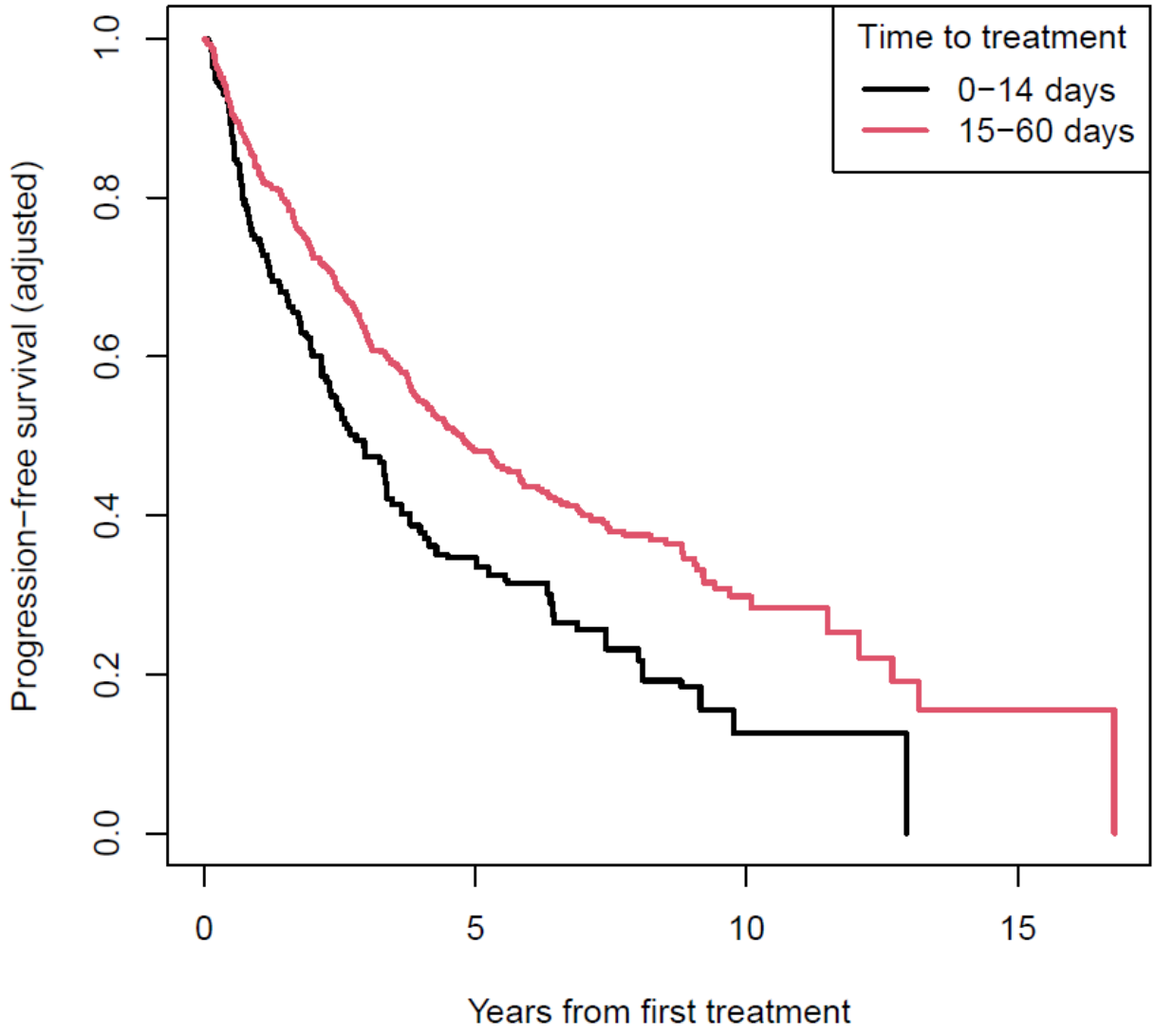
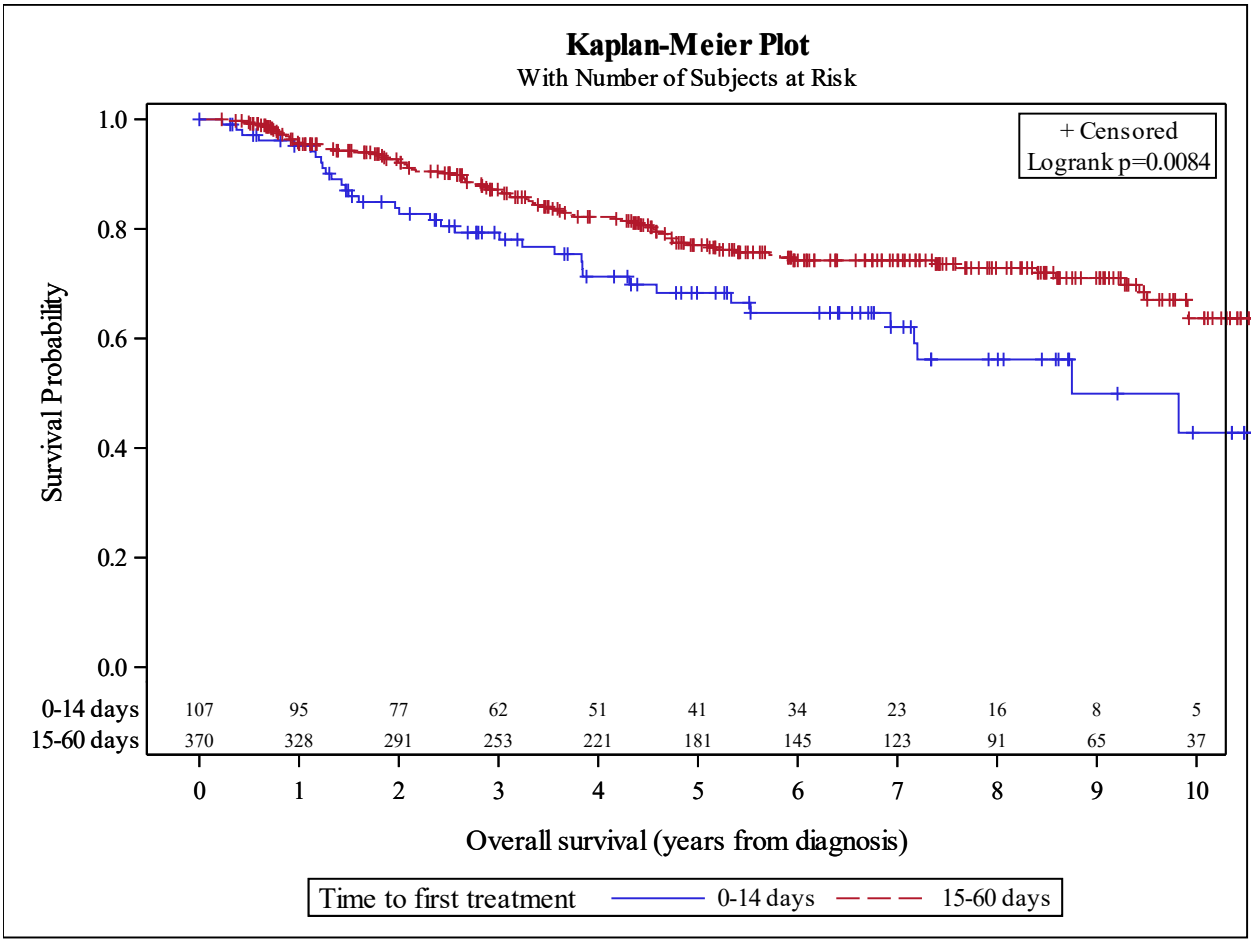


Figure S3: OS between short DTI and long DTI among the recipients of intensive induction therapy



Time to first treatment	No. of Subject	Event	Censored	Median Survival (95% CI)	Time to first treatment	2 Yr Survival	5 Yr Survival
0-14 days	107	35 (33%)	72 (67%)	8.8 (6.9, NA)	0-14 days	83.8% (74.9%, 89.8%)	68.3% (57.2%, 77.1%)
15-60 days	370	86 (23%)	284 (77%)	NA (11.6, NA)	15-60 days	92.1% (88.7%, 94.5%)	77.0% (71.8%, 81.5%)

Figure S4. Adjusted OS

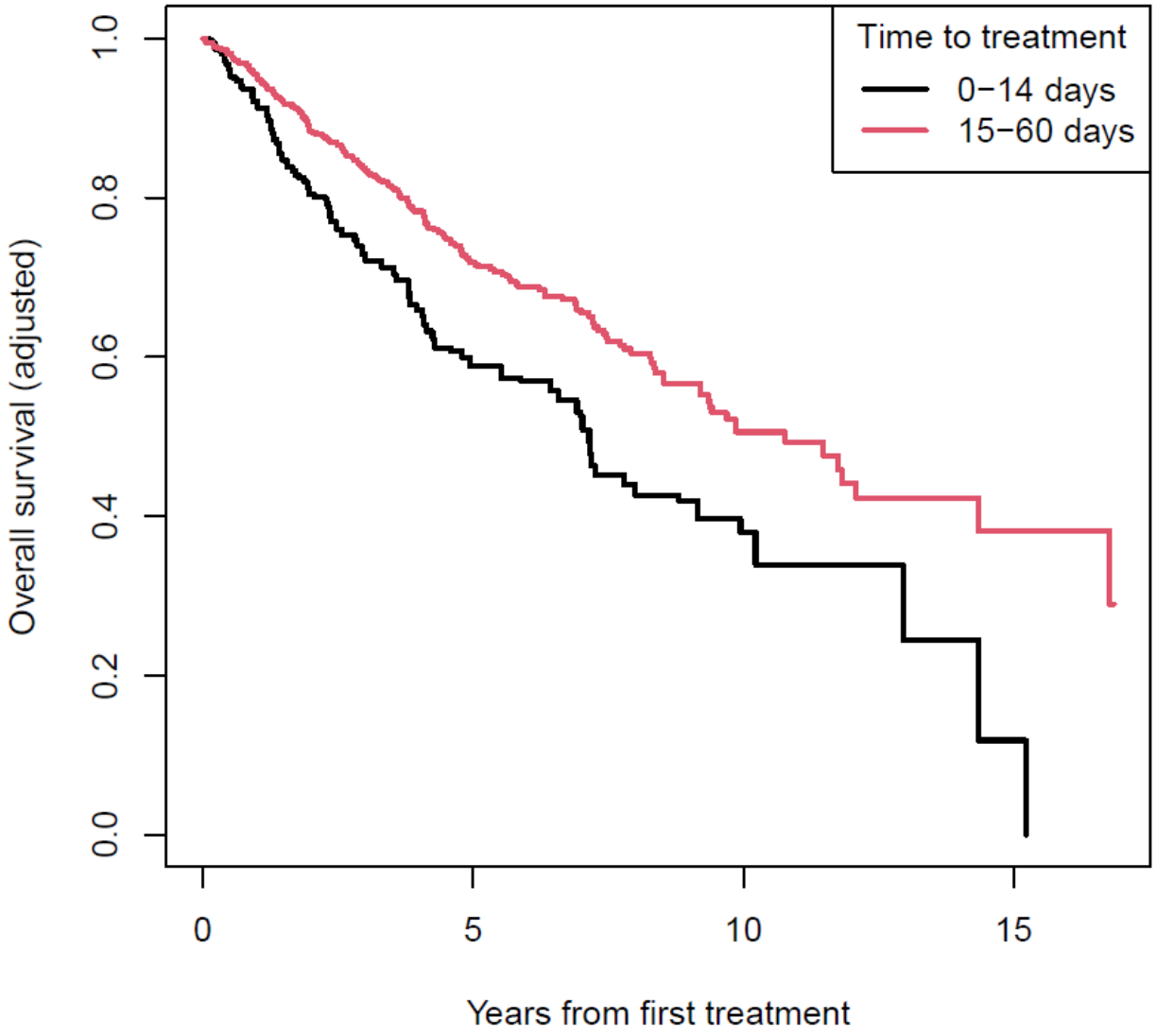
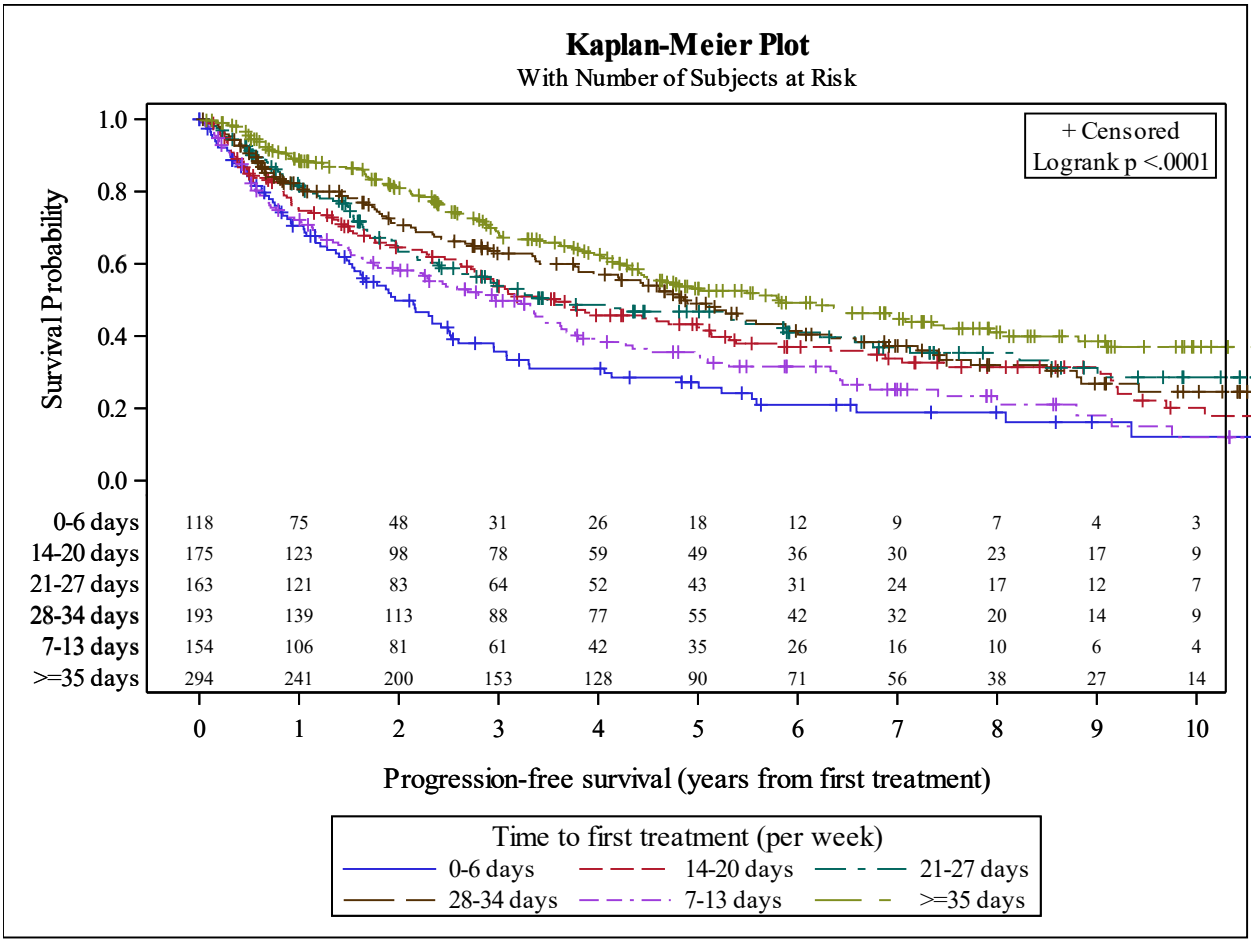
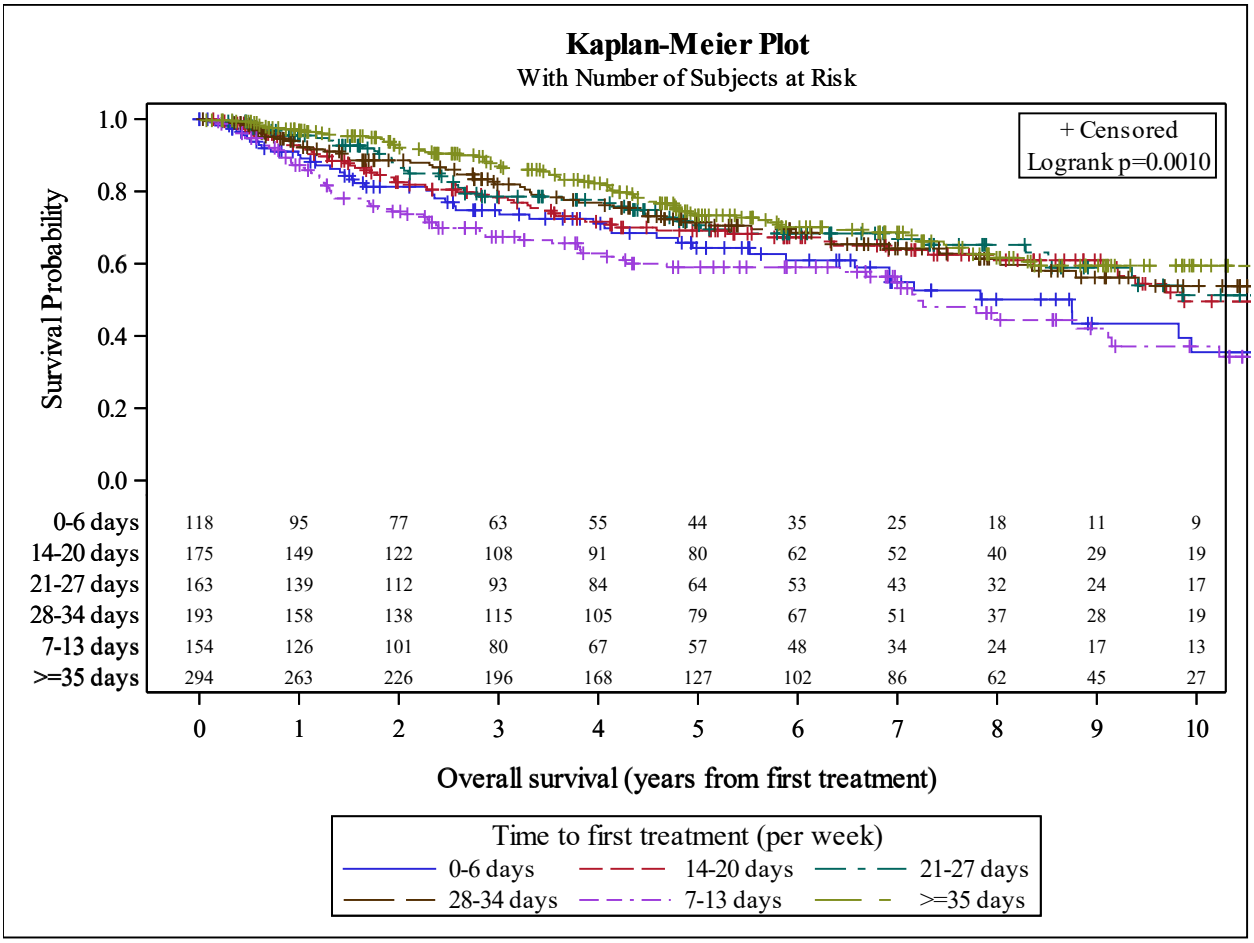


Figure S5. DTI in weeks - PFS



Time to first treatment (per week)	No. of Subject	Event	Censored	Median Survival (95% CI)	DTI (per week)	2 Yr Survival	5 Yr Survival
0-6 days	118	83 (70%)	35 (30%)	2 (1.5, 2.5)	0-6 days	49.8% (39.9%, 58.9%)	27.2% (18.6%, 36.6%)
7-13 days	154	104 (68%)	50 (32%)	3 (2, 3.7)	7-13 days	58.2% (49.8%, 65.7%)	34.6% (26.4%, 42.9%)
14-20 days	175	112 (64%)	63 (36%)	3.6 (2.8, 5)	14-20 days	64.6% (56.7%, 71.3%)	42.4% (34.4%, 50.2%)
21-27 days	163	87 (53%)	76 (47%)	3.5 (2.6, 5.9)	21-27 days	63.4% (54.9%, 70.7%)	46.8% (38.0%, 55.1%)
28-34 days	193	103 (53%)	90 (47%)	4.9 (3.8, 5.9)	28-34 days	71.3% (64.0%, 77.4%)	49.0% (40.7%, 56.7%)
>=35 days	294	135 (46%)	159 (54%)	5.8 (4.5, 7.5)	>=35 days	80.9% (75.7%, 85.1%)	53.1% (46.4%, 59.4%)

Figure S6. DTI in weeks - OS



Time to first treatment (per week)	No. of Subject	Event	Censored	Median Survival (95% CI)	DTI (per week)	2 Yr Survival	5 Yr Survival
0-6 days	118	46 (39%)	72 (61%)	8.8 (5.9, 15.2)	0-6 days	81.3% (72.5%, 87.5%)	64.4% (53.6%, 73.3%)
7-13 days	154	70 (45%)	84 (55%)	7.2 (4.7, 9.1)	7-13 days	74.4% (66.5%, 80.8%)	59.0% (50.0%, 67.0%)
14-20 days	175	61 (35%)	114 (65%)	9.9 (9.2, NA)	14-20 days	82.6% (75.7%, 87.6%)	69.2% (61.0%, 76.0%)
21-27 days	163	51 (31%)	112 (69%)	10.8 (8.5, NA)	21-27 days	86.5% (79.6%, 91.2%)	70.6% (61.6%, 77.9%)
28-34 days	193	60 (31%)	133 (69%)	11.3 (8, NA)	28-34 days	88.6% (82.9%, 92.5%)	71.5% (63.4%, 78.0%)
>=35 days	294	81 (28%)	213 (72%)	12.1 (11.8, NA)	>=35 days	92.1% (88.1%, 94.8%)	73.3% (66.9%, 78.7%)

Figure S7. Spline curves