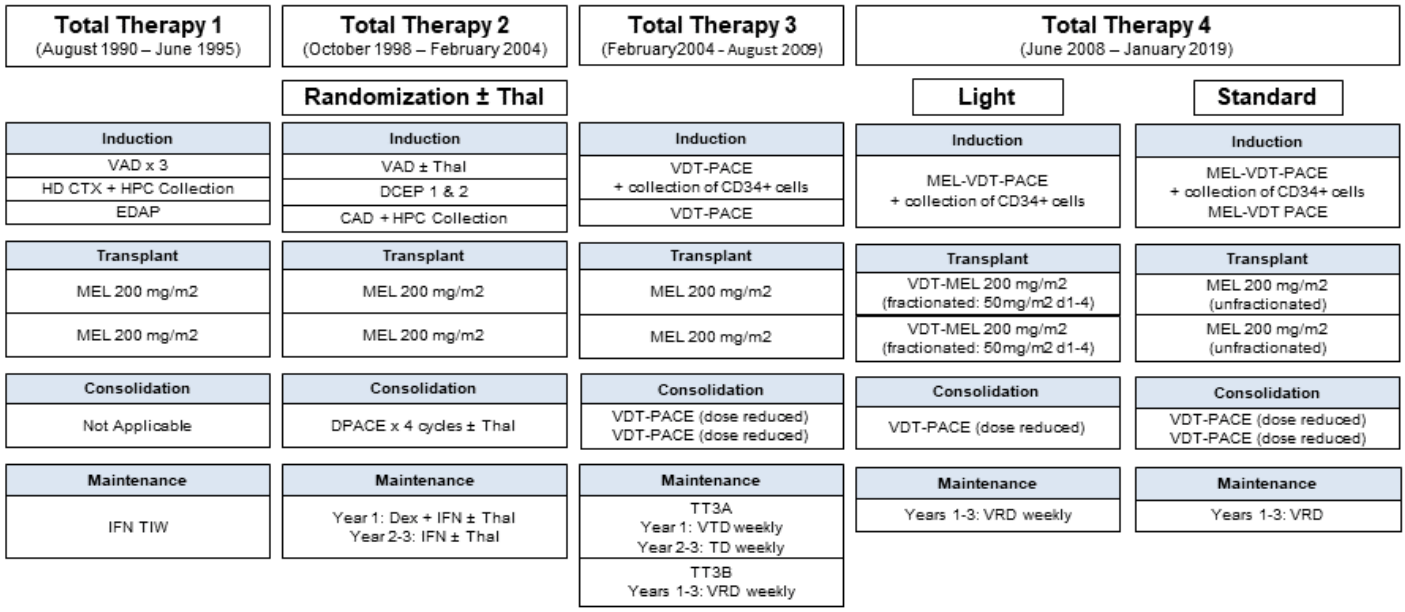
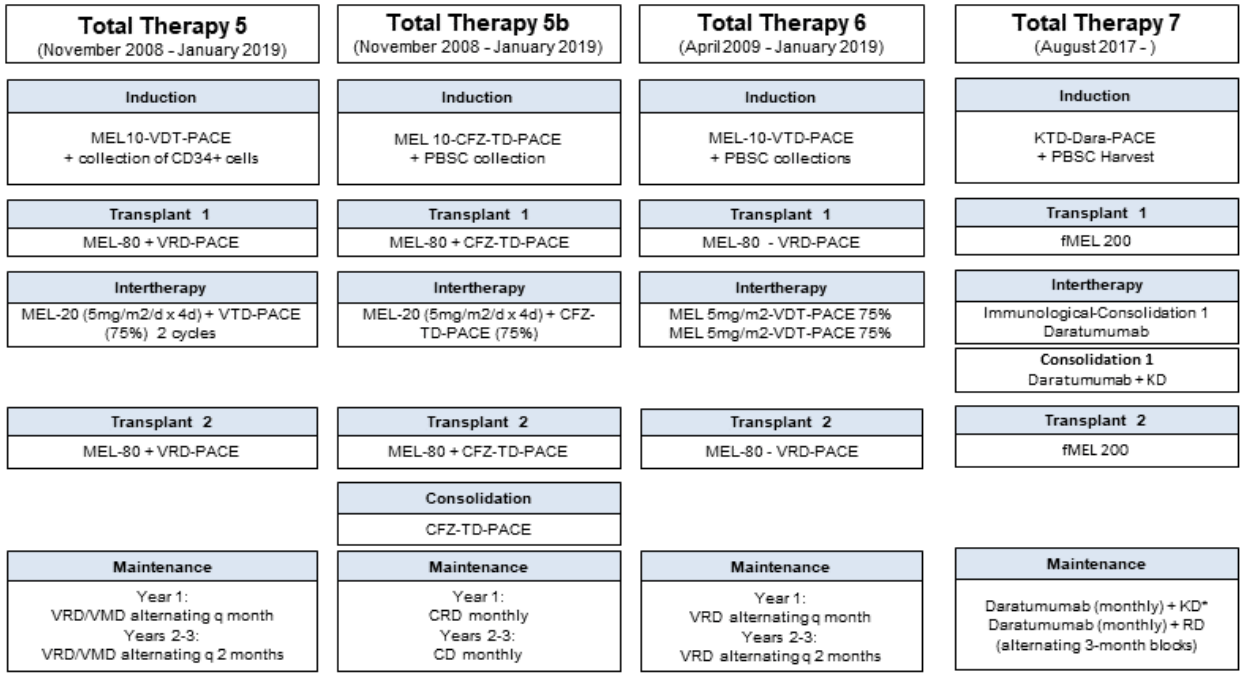
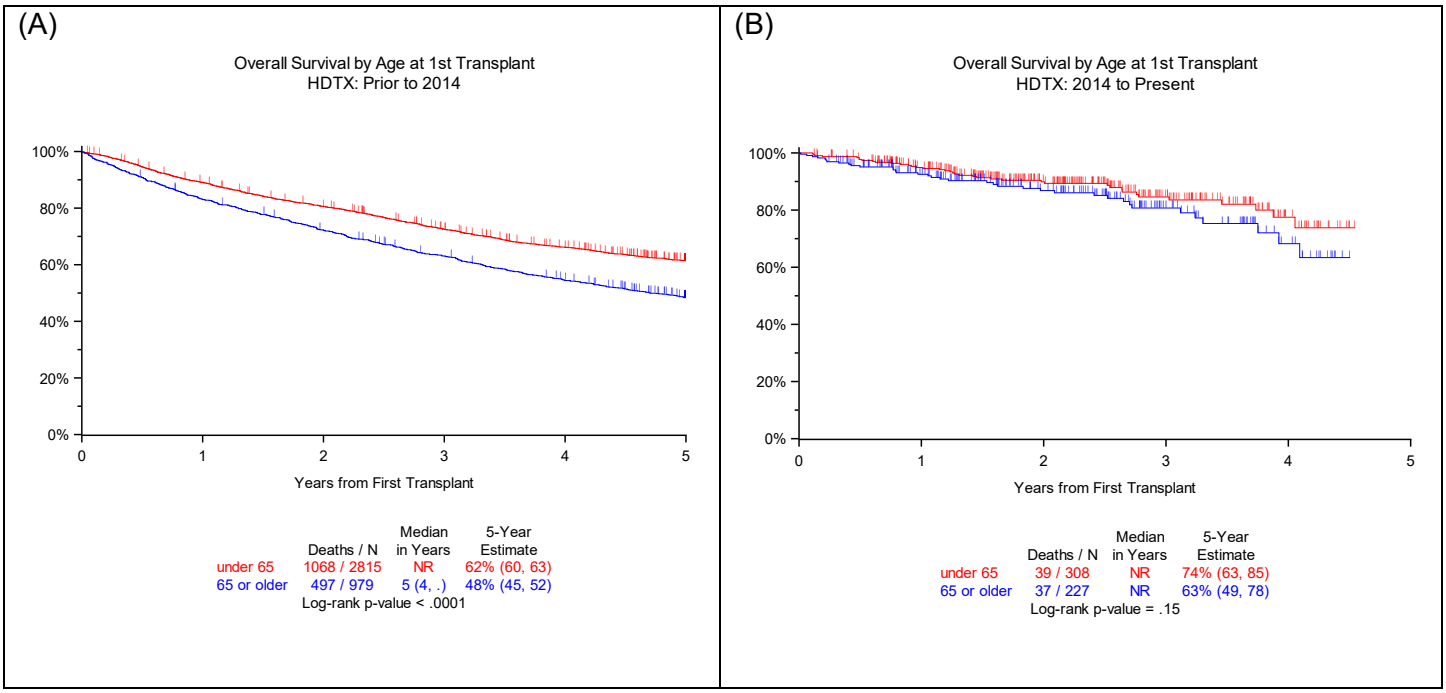
Supplemental Figure 1. Total Therapy Schemas





VDT-PACE: bortezomib (Velcade), dexamethasone, thalidomide, cisplatin (Platinum), doxorubicin (Adriamycin), cyclophosphamide, etoposide; MEL: melphalan; VTD: bortezomib (Velcade), thalidomide, dexamethasone; TD: thalidomide, dexamethasone; MEL-VDT-PACE: melphalan, bortezomib (Velcade), dexamethasone, thalidomide, cisplatin (Platinum), doxorubicin (Adriamycin), cyclophosphamide, etoposide; VDT-MEL: bortezomib (Velcade), dexamethasone, thalidomide, melphalan; VRD: bortezomib (Velcade), lenalidomide (Revlimid), dexamethasone; VMD: bortezomib (Velcade), melphalan, dexamethasone; CRD: carfilzomib, Revlimid®, dexamethasone; CD: carfilzomib + dexamethasone; fMEL: fractionated melphalan; KD: carfilzomib and dexamethasone; RD: lenalidomide and dexamethasone.

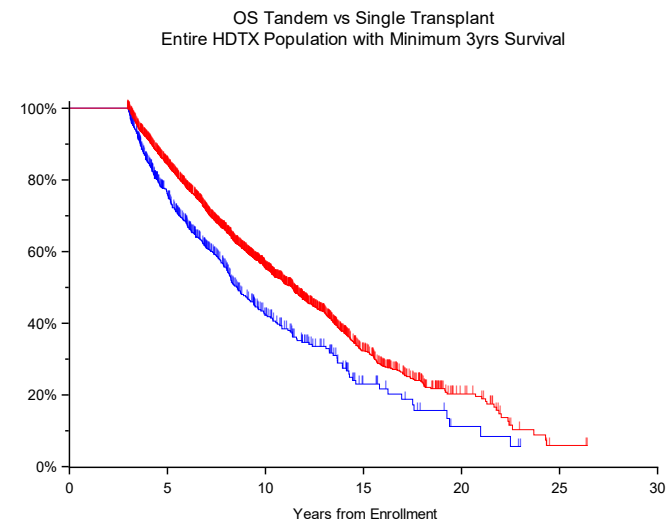
Supplemental Figure 2. OS Kaplan-Meier Curves in Transplant Eligible Patients.



(A) OS Kaplan-Meier Restricted to Patients with 1st ASCT Prior to 2014. (B) OS Kaplan-Meier Restricted to Patients with 1st ASCT in 2014 or Later.

Supplemental Figure 3. Kaplan-Meier Curves for Single vs Tandem Transplant.

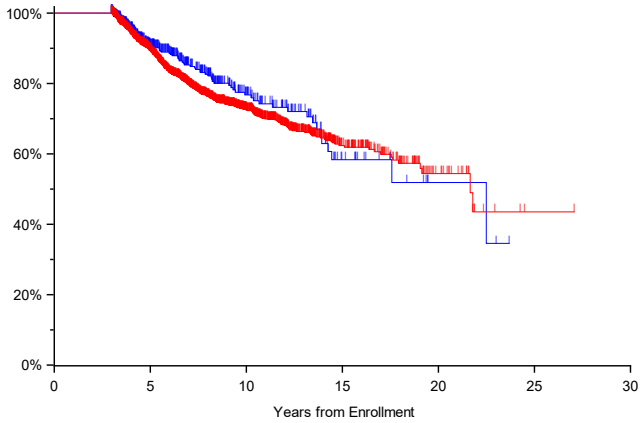
(A)



	Events / N	Median in Years	5-Year Estimate
Single Transplant	290 / 564	9 (8, 9)	76% (72, 80)
Tandem Transplant	1122 / 2193	11 (11, 12)	84% (83, 86)

Log-rank p-value < .0001

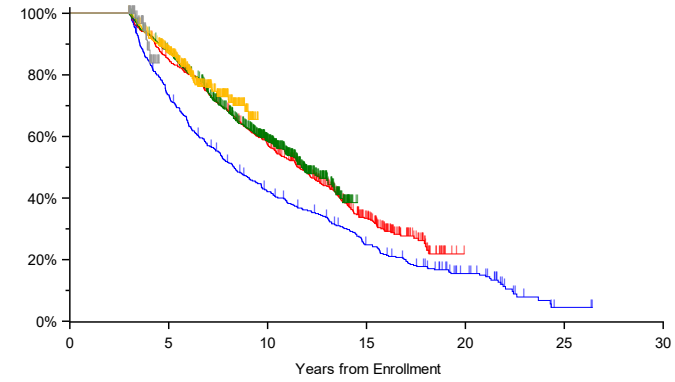
(B)



	Events / N	Median in Years	5-Year Estimate
Single Transplant	87 / 544	22 (14, .)	91% (88, 93)
Tandem Transplant	488 / 2011	22 (19, .)	89% (88, 91)

Log-rank p-value = .12

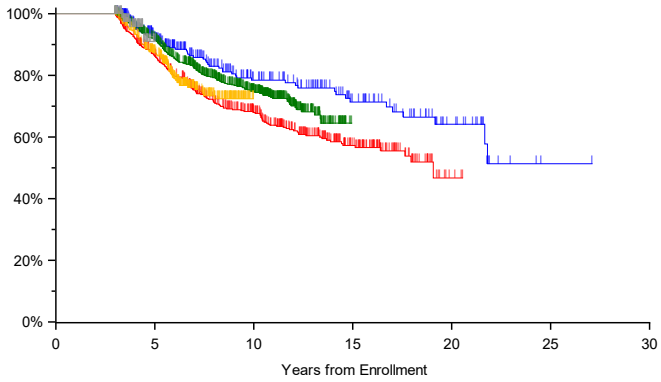
(C)



	Events / N	Median in Years	5-Year Estimate
1997 or Earlier	305 / 362	8 (7, 9)	74% (69, 78)
1998-2003	362 / 559	12 (11, 12)	85% (82, 88)
2004-2008	356 / 780	12 (11, 13)	88% (86, 90)
2009-2013	93 / 410	NR	87% (84, 90)
2014 or Later	6 / 82	NR	84% (71, 97)

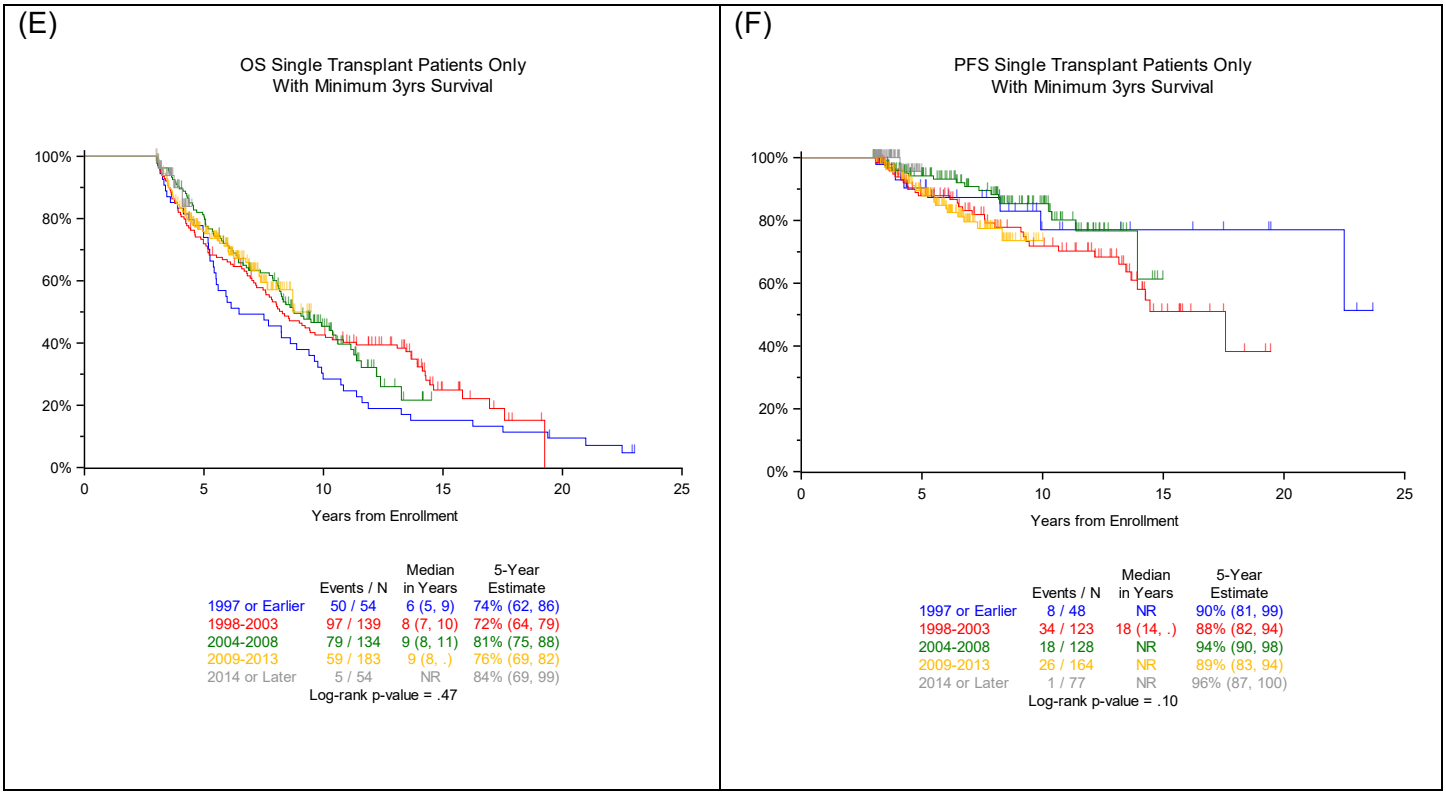
Log-rank p-value < .0001

(D)



	Events / N	Median in Years	5-Year Estimate
1997 or Earlier	59 / 306	NR	92% (88, 95)
1998-2003	175 / 497	19 (16, .)	86% (83, 89)
2004-2008	172 / 740	NR	91% (89, 94)
2009-2013	78 / 364	NR	87% (84, 91)
2014 or Later	4 / 104	NR	91% (81, 100)

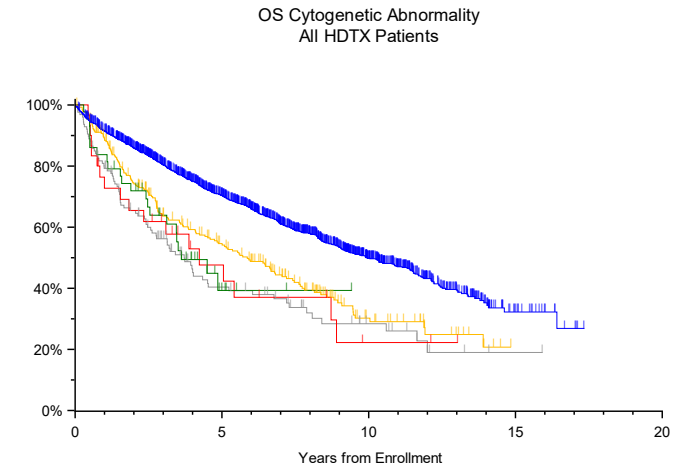
Log-rank p-value = .0007



(A) OS Kaplan-Meier with 3-year landmark comparing single vs tandem transplant patients. (B) PFS Kaplan-Meier with 3-year landmark comparing single vs tandem transplant patients only. (C) OS Kaplan-Meier with 3-year landmark restricted to tandem transplant patients only. (D) PFS Kaplan-Meier with 3-year landmark restricted to tandem transplant patients only. (E) OS Kaplan-Meier with 3-year landmark restricted to single transplant patients only. (F) PFS Kaplan-Meier with 3-year landmark restricted to single transplant patients only.

Supplemental Figure 4. Kaplan-Meier Curves for Single vs Tandem Transplant

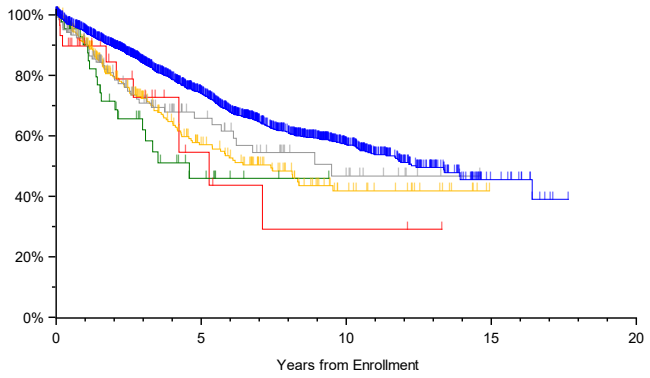
(A)



	Events / N	Median in Years	5-Year Estimate
t(4;14)	154 / 270	6 (5, 7)	55% (48, 61)
t(14;16)	77 / 126	4 (3, 5)	40% (31, 50)
t(14;20)	18 / 30	4 (2, 9)	48% (28, 67)
17p del	22 / 43	4 (3, .)	39% (21, 57)
No high risk abnormalities	703 / 1700	10 (9, 11)	70% (68, 73)

Log-rank p-value < .0001

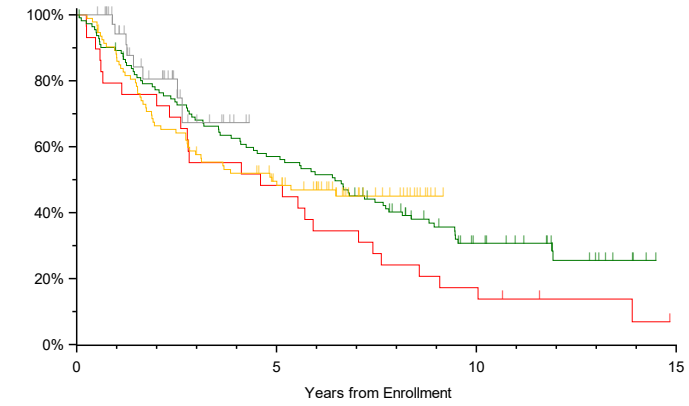
(B)



	Events / N	Median in Years	5-Year Estimate
t(4;14)	104 / 267	7 (5, .)	57% (50, 64)
t(14;16)	38 / 123	9 (6, .)	66% (55, 76)
t(14;20)	10 / 29	5 (4, .)	55% (28, 81)
17p del	18 / 43	5 (3, .)	46% (28, 64)
No high risk abnormalities	524 / 1685	12 (11, .)	74% (72, 76)

Log-rank p-value < .0001

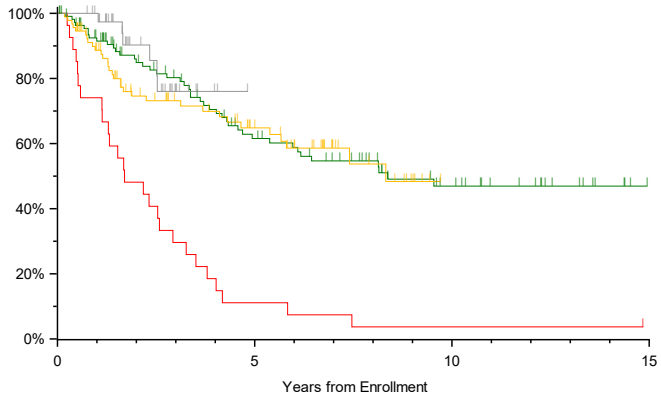
(C)



	Events / N	Median in Years	5-Year Estimate
1998-2003	26 / 29	5 (3, 7)	48% (30, 66)
2004-2008	75 / 112	6 (4, 8)	57% (48, 66)
2009-2013	49 / 93	5 (3, .)	50% (39, 60)
2014 or Later	8 / 41	NR	67% (47, 88)

Log-rank p-value = .17

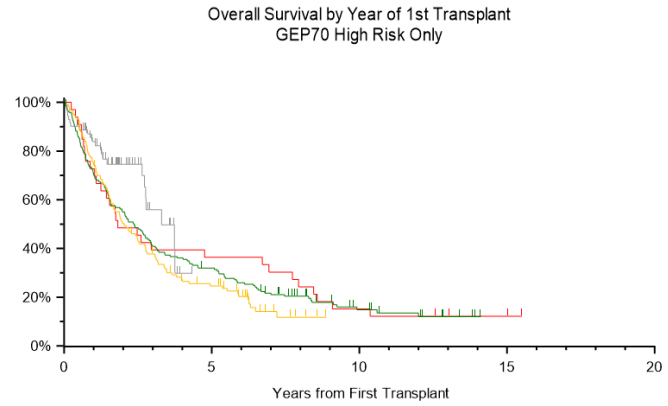
(D)



	Events / N	Median in Years	5-Year Estimate
1998-2003	26 / 27	2 (1, 3)	11% (0, 23)
2004-2008	43 / 112	8 (5, .)	62% (51, 72)
2009-2013	32 / 92	8 (6, .)	65% (54, 76)
2014 or Later	6 / 41	NR	76% (59, 93)

Log-rank p-value < .0001

(E)

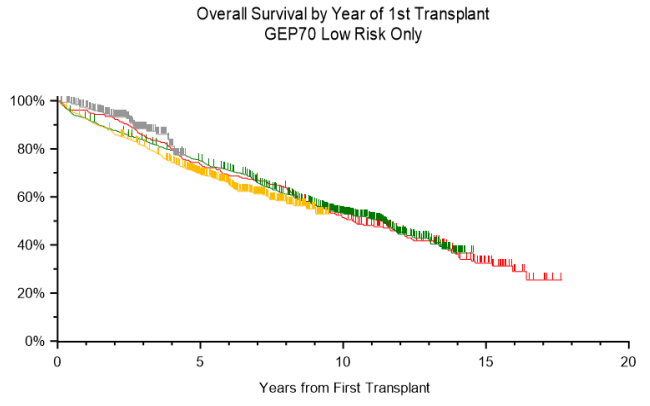


	Deaths / N	Median in Years	5-Year Estimate
1998-2003	29 / 33	2 (1, 7)	36% (20, 53)
2004-2008	142 / 170	2 (2, 3)	32% (25, 39)
2009-2013	100 / 124	2 (2, 3)	25% (17, 32)
2014 or Later	23 / 71	3 (3, .)	30% (5, 54)

Log-rank p-value = .09

Pairwise p-value	1997 or Earlier	1998-2003	2004-2008	2009-2013	2014 or Later
1997 or Earlier	-				
1998-2003	NA	-			
2004-2008	NA	0.75	-		
2009-2013	NA	0.22	0.30	-	
2014 or Later	NA	0.26	0.06	0.03	-

(F)



	Deaths / N	Median in Years	5-Year Estimate
1998-2003	145 / 230	10 (9, 12)	73% (68, 79)
2004-2008	348 / 706	11 (10, 12)	75% (72, 78)
2009-2013	217 / 591	NR	70% (66, 73)
2014 or Later	30 / 311	NR	77% (67, 88)

Log-rank p-value = .03

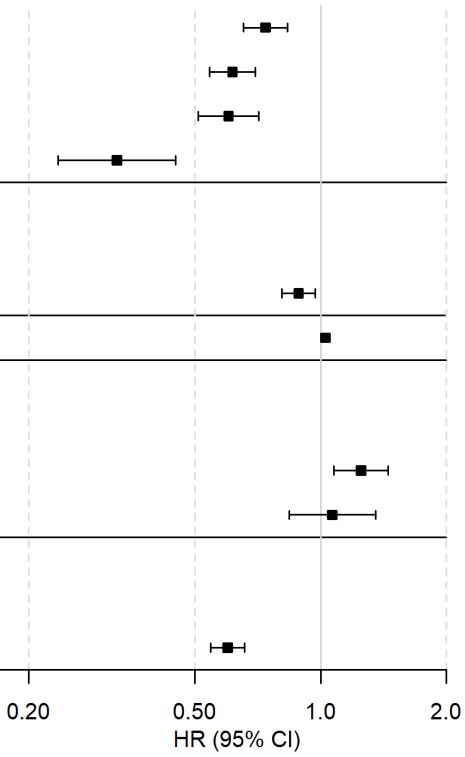
Pairwise p-value	1997 or Earlier	1998-2003	2004-2008	2009-2013	2014 or Later
1997 or Earlier	-				
1998-2003	NA	-			
2004-2008	NA	0.90	-		
2009-2013	NA	0.22	0.11	-	
2014 or Later	NA	0.52	0.05	0.007	-

(A) OS Kaplan-Meier comparing cytogenetic abnormalities. (B) PFS Kaplan-Meier comparing cytogenetic abnormalities. (C) OS Kaplan-Meier among t(4;14) patients only. (D) PFS Kaplan-Meier among t(4;14) patients only. (E) OS Kaplan-Meier Restricted to GEP70 High Risk Only. (F) OS Kaplan-Meier Restricted to GEP70 Low Risk Only.

Supplemental Figure 5A. Cox Proportional Hazard Model in Restricted to Patients Less than 65 Years Old

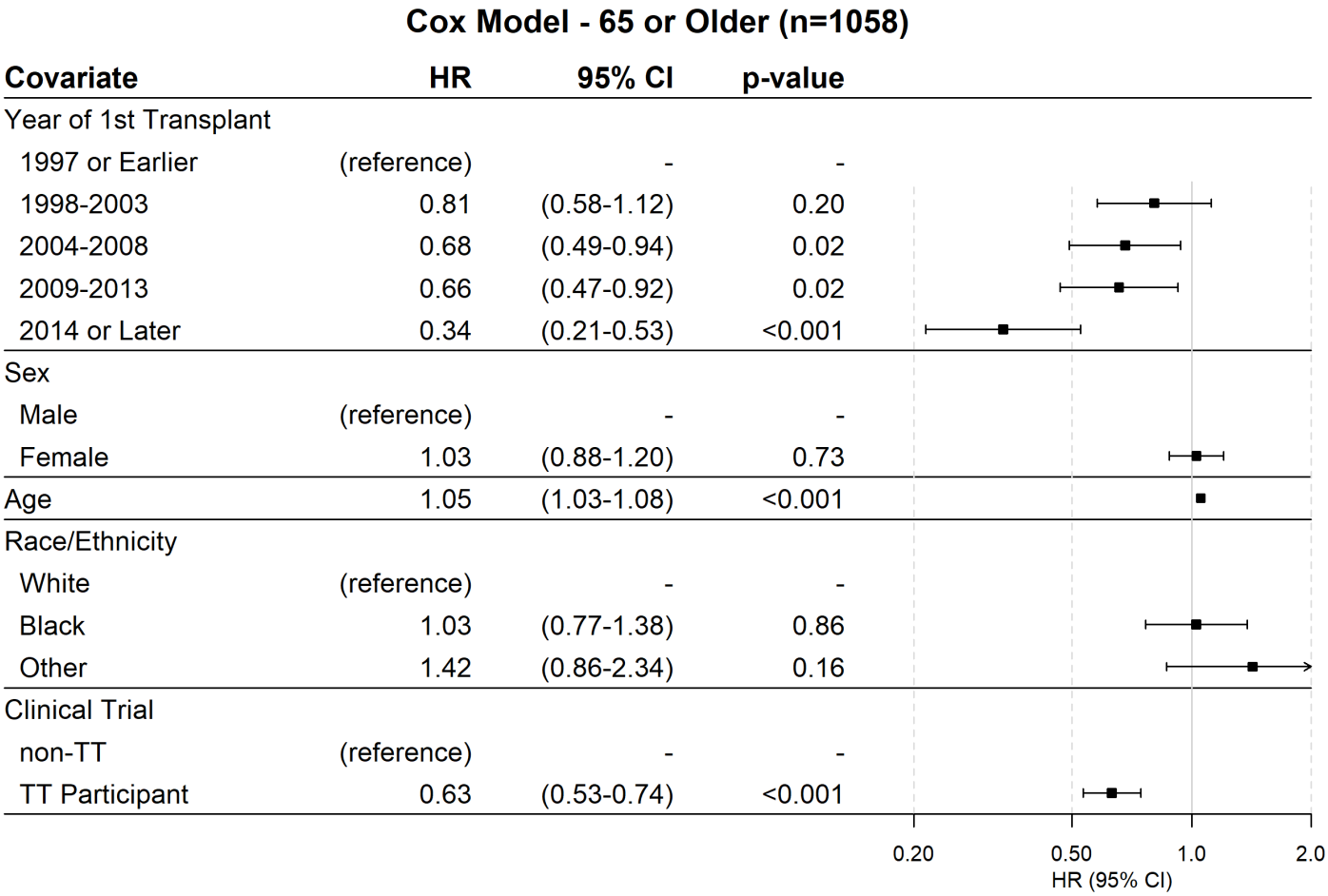
Cox Model - Less Than 65 Years Old (n=3271)

Covariate	HR	95% CI	p-value
Year of 1st Transplant			
1997 or Earlier	(reference)	-	-
1998-2003	0.74	(0.65-0.83)	<0.001
2004-2008	0.62	(0.54-0.70)	<0.001
2009-2013	0.60	(0.51-0.71)	<0.001
2014 or Later	0.33	(0.24-0.45)	<0.001
Sex			
Male	(reference)	-	-
Female	0.88	(0.81-0.97)	0.01
Age	1.03	(1.02-1.03)	<0.001
Race/Ethnicity			
White	(reference)	-	-
Black	1.25	(1.07-1.45)	<0.001
Other	1.07	(0.84-1.35)	0.60
Clinical Trial			
non-TT	(reference)	-	-
TT Participant	0.60	(0.55-0.66)	<0.001



HR=Hazard Ratio, CI=Confidence Interval, TT=Total Therapy Trial

Supplemental Figure 5B. Cox Proportional Hazard Model in Restricted to Patients Less 65 or Older

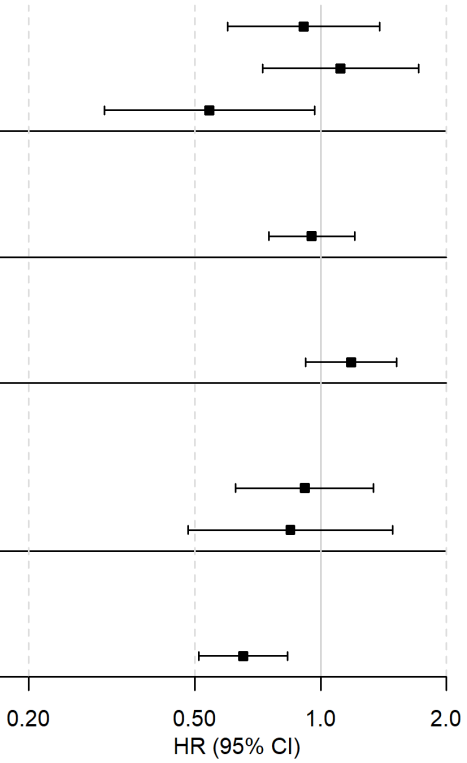


HR=Hazard Ratio, CI=Confidence Interval, TT=Total Therapy Trial

Supplemental Figure 5C. Cox Proportional Hazard Model in Restricted to GEP70 High Risk Patients

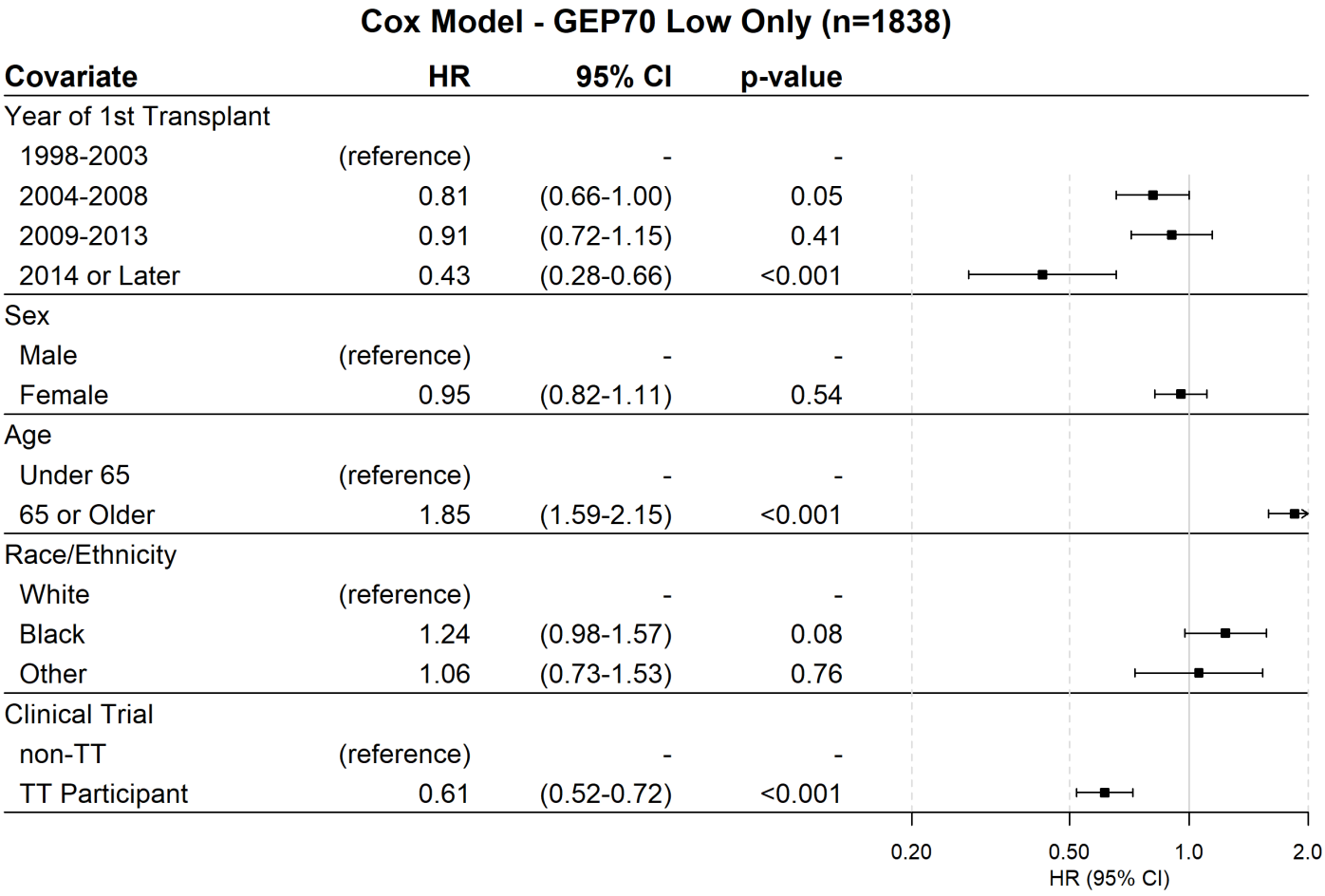
Cox Model - GEP70 High Only (n=398)

Covariate	HR	95% CI	p-value
Year of 1st Transplant			
1998-2003	(reference)	-	-
2004-2008	0.91	(0.60-1.38)	0.66
2009-2013	1.12	(0.73-1.71)	0.62
2014 or Later	0.54	(0.30-0.97)	0.04
Sex			
Male	(reference)	-	-
Female	0.95	(0.75-1.21)	0.68
Age			
Under 65	(reference)	-	-
65 or Older	1.18	(0.92-1.52)	0.19
Race/Ethnicity			
White	(reference)	-	-
Black	0.91	(0.63-1.34)	0.65
Other	0.85	(0.48-1.49)	0.56
Clinical Trial			
non-TT	(reference)	-	-
TT Participant	0.65	(0.51-0.83)	<0.001



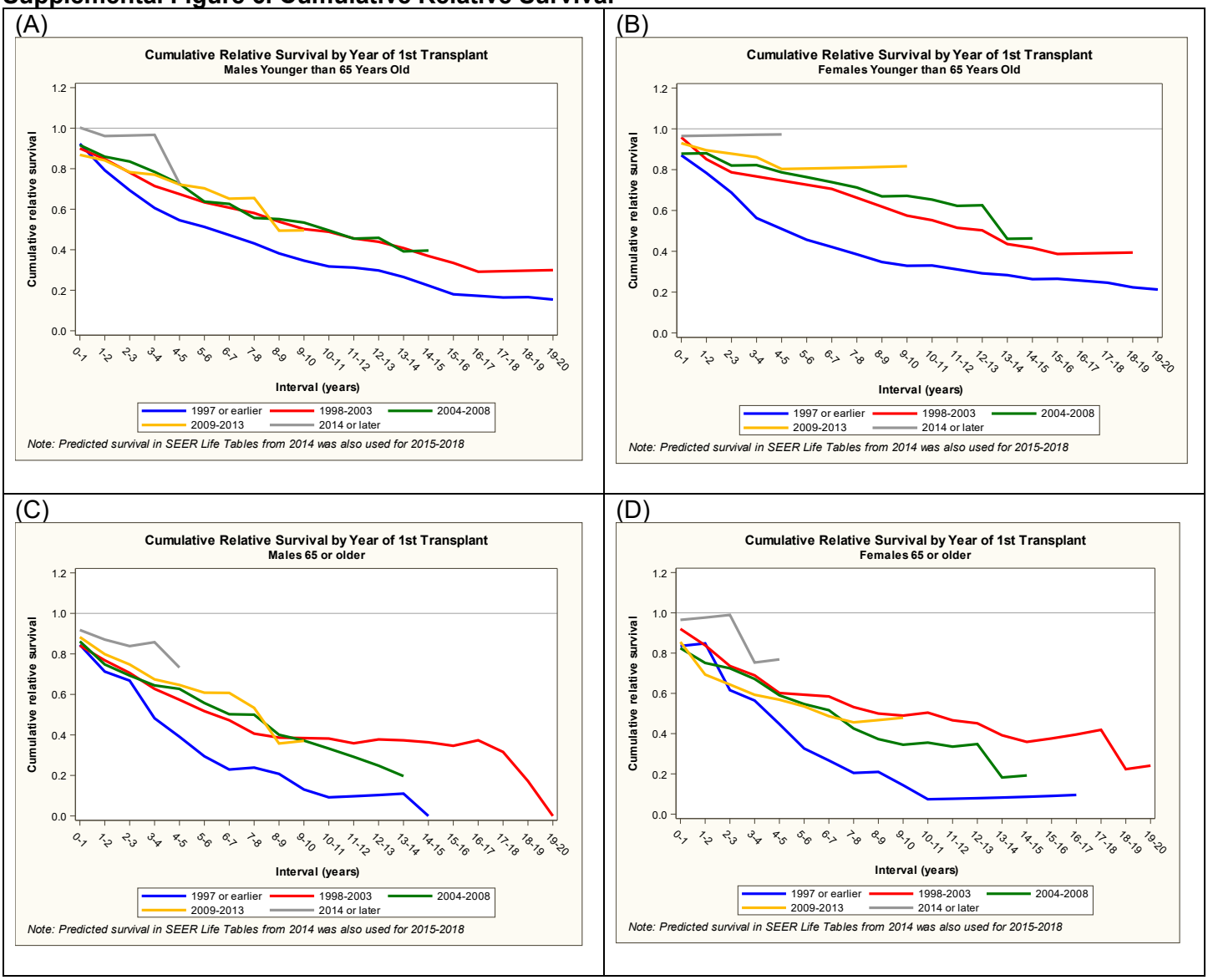
HR=Hazard Ratio, CI=Confidence Interval, TT=Total Therapy Trial

Supplemental Figure 5D. Cox Proportional Hazard Model in Restricted to GEP70 Low Risk Patients



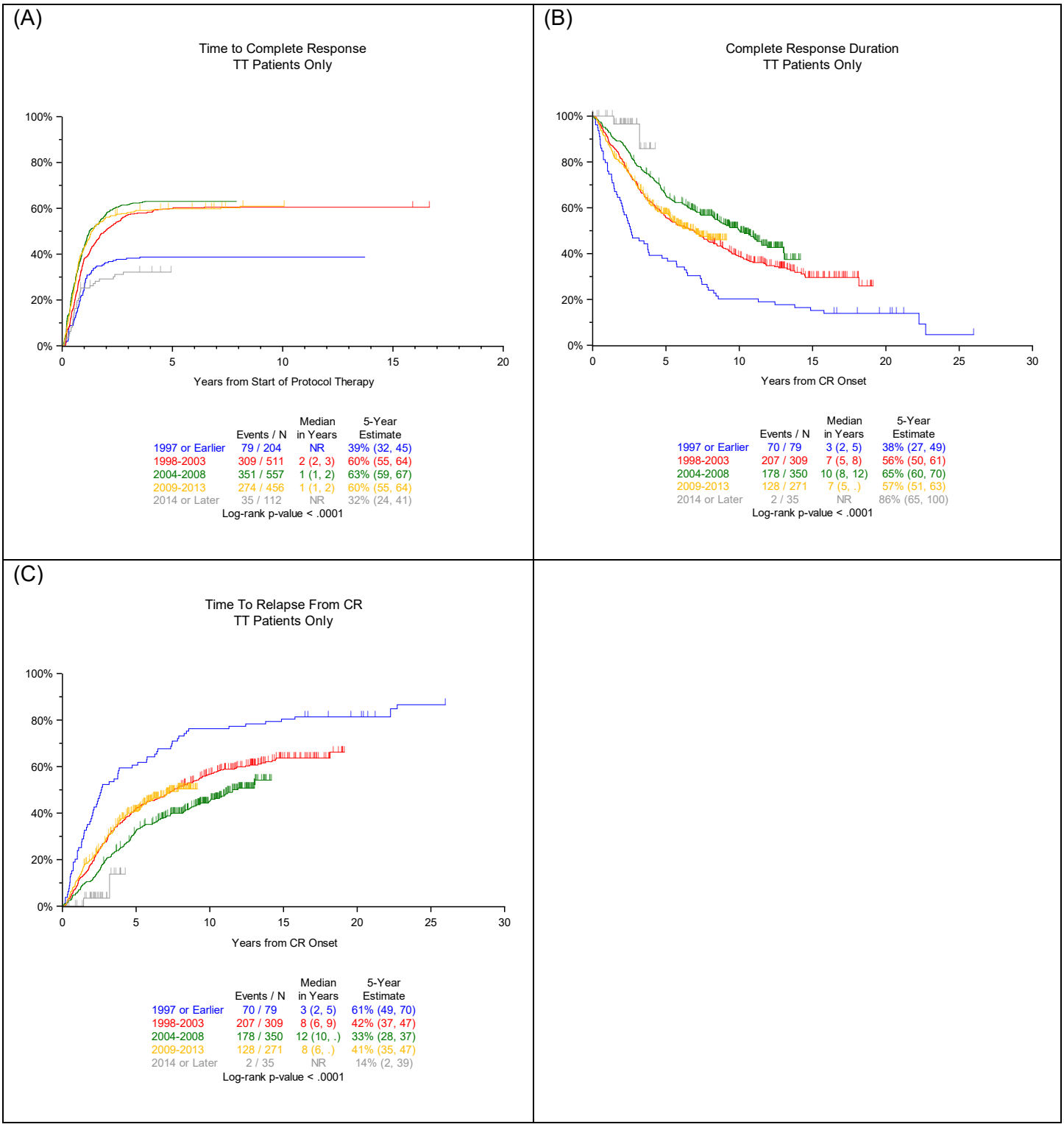
HR=Hazard Ratio, CI=Confidence Interval, TT=Total Therapy Trial

Supplemental Figure 6. Cumulative Relative Survival



(A) Cumulative relative survival restricted to males younger than 65 years old (n=1889). (B) Cumulative relative survival restricted to females younger than 65 years old (n=1234). (C) Cumulative relative survival restricted to males 65 or older (n=757). (D) Cumulative relative survival restricted to females 65 or older (n=449). Cumulative relative survival shows the ratio of the observed survival in the UAMS cohort, relative to the normal expected survival in the SEER Life Tables, matched on age, sex, year, and race/ethnicity. Lines that near 1.0 would indicate that UAMS survival is approaching the rates of SEER survival, where the excess mortality due to MM for a given year interval is approaching 0. Downward sloping lines indicate consecutive years of follow-up where UAMS survival was worse compared to SEER survival, while lines that plateau would indicate years when the UAMS survival was similar to SEER survival.

Supplemental Figure 7. Complete Response (CR) or Better Among TT Patients



(A) Time to achieve Complete Response (CR) or better among TT patients. (B) Duration of CR among TT patients. (C) Time to relapse or death among patients who achieved CR or better.