

## Supplemental Online Content

Hallemeier CL, Moughan J, Haddock MG, et al. Association of radiotherapy duration with clinical outcomes in patients with esophageal cancer treated in NRG oncology trials: a secondary analysis of NRG Oncology Randomized Clinical Trials. *JAMA Netw Open*. 2023;6(4):e238504. doi:10.1001/jamanetworkopen.2023.8504

**eTable 1.** Characteristics by RT Duration  $\leq 45$  Days vs  $> 45$  Days

**eTable 2.** Characteristics by RT Duration  $\leq 39$  Days vs  $> 39$  Days

**eTable 3.** Characteristics by RT Interruptions

**eTable 4.** RT Duration  $\leq 45$  Days vs  $> 45$  Days, Controlling for NRG Oncology Trial

**eTable 5.** RT Duration  $\leq 45$  Days vs  $> 45$  Days in Patients with Squamous Cell Carcinoma Histology

**eTable 6.** RT Duration  $\leq 45$  Days vs  $> 45$  Days in Patients with Adenocarcinoma Histology

**eTable 7.** RT Duration (Continuous), Controlling for NRG Oncology Trial

**eTable 8.** RT Duration  $\leq 39$  Days vs  $> 39$  Days, Controlling for NRG Oncology Trial

**eTable 9.** Multivariable Models: RT Duration ( $\leq 39$  Days vs.  $> 39$  Days)

**eTable 10.** RT Interruptions, Controlling for NRG Oncology Trial

**eFigure 1.** Outcomes for RT Duration Dichotomized by XTile Cutpoint

**eFigure 2.** Outcomes for RT Duration Dichotomized by Median

**eFigure 3.** Outcomes for RT Interruption

This supplemental material has been provided by the authors to give readers additional information about their work.

**eTable 1: Characteristics by RT Duration ≤45 days vs >45 days**

Pretreatment, Tumor, or Treatment Characteristics	≤45 days	>45 days	p-value <sup>a</sup>
	(n=446)	(n=63)	
Age (years)			
Median (IQR)	64 (57-70)	62 (54-69)	
Min-Max	38-87	32-83	
Sex			0.02
Male	373 (84%)	45 (71%)	
Female	73 (16%)	18 (29%)	
Race			0.05
Non-white	110 (25%)	23 (37%)	
White	336 (75%)	40 (63%)	
Zubrod			0.23
0	227 (51%)	27 (43%)	
1 or 2	219 (49%)	36 (57%)	
Histology			0.97
Adenocarcinoma	190 (43%)	27 (43%)	
Squamous	256 (57%)	36 (57%)	
Tumor Size			0.02
< 5 cm	172 (39%)	15 (24%)	
≥ 5 cm	274 (61%)	48 (76%)	
T Stage			0.47
T1/T2	163 (37%)	26 (41%)	
T3/T4/Unknown	283 (63%)	37 (59%)	
N Stage			0.34
N0	234 (52%)	29 (46%)	
N1/NX	212 (48%)	34 (54%)	
≥80% of Protocol-Specified Concurrent Chemo			0.02
No	32 (7%)	10 (16%)	
Yes	414 (93%)	53 (84%)	
Trial			0.87
NRG/RTOG 0436	251 (56%)	36 (57%)	
NRG/RTOG 8501	104 (23%)	13 (21%)	
NRG/RTOG 9405	91 (20%)	14 (22%)	

Data are n (%) unless otherwise indicated.

Abbreviations: RT, radiation therapy; IQR, interquartile range; min, minimum; max, maximum; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group

<sup>a</sup>p-value from Chi-square/Fisher's Exact Test

**eTable 2: Characteristics by RT Duration ≤39 days vs >39 days**

Pretreatment, Tumor, or Treatment Characteristics	≤39 days	>39 days	p-value <sup>a</sup>
	(n=271)	(n=238)	
Age (years)			
Median (IQR)	64 (58-70)	64 (56-70)	
Min-Max	38-87	32-83	
Sex			0.08
Male	230 (85%)	188 (79%)	
Female	41 (15%)	50 (21%)	
Race			0.003
Non-white	56 (21%)	77 (32%)	
White	215 (79%)	161 (68%)	
Zubrod			0.17
0	143 (53%)	111 (47%)	
1 or 2	128 (47%)	127 (53%)	
Histology			0.53
Adenocarcinoma	119 (44%)	98 (41%)	
Squamous	152 (56%)	140 (59%)	
Tumor Size			0.17
< 5 cm	107 (39%)	80 (34%)	
≥ 5 cm	164 (61%)	158 (66%)	
T Stage			0.80
T1/T2	102 (38%)	87 (37%)	
T3/T4/Unknown	169 (62%)	151 (63%)	
N Stage			0.38
N0	145 (54%)	118 (50%)	
N1/NX	126 (46%)	120 (50%)	
≥80% of Protocol-Specified Concurrent Chemo			0.04
No	16 (6%)	26 (11%)	
Yes	255 (94%)	212 (89%)	
Trial			0.24
NRG/RTOG 0436	152 (56%)	135 (57%)	
NRG/RTOG 8501	69 (25%)	48 (20%)	
NRG/RTOG 9405	50 (18%)	55 (23%)	

Data are n (%) unless otherwise indicated.

Abbreviations: RT, radiation therapy; IQR, interquartile range; min, minimum; max, maximum; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group

<sup>a</sup>p-value from Chi-square/Fisher's Exact Test

**eTable 3: Characteristics by RT Interruptions**

Pretreatment, Tumor, or Treatment Characteristics	No	Yes	p-value <sup>a</sup>
	(n=302)	(n=207)	
Age (years)			
Median (IQR)	64 (57-70)	64 (57-70)	
Min-Max	38-87	32-83	
Sex			0.06
Male	256 (85%)	162 (78%)	
Female	46 (15%)	45 (22%)	
Race			0.04
Non-white	69 (23%)	64 (31%)	
White	233 (77%)	143 (69%)	
Zubrod			0.02
0	164 (54%)	90 (43%)	
1 or 2	138 (46%)	117 (57%)	
Histology			0.82
Adenocarcinoma	130 (43%)	87 (42%)	
Squamous	172 (57%)	120 (58%)	
Tumor Size			0.01
< 5 cm	124 (41%)	63 (30%)	
≥ 5 cm	178 (59%)	144 (70%)	
T Stage			0.83
T1/T2	111 (37%)	78 (38%)	
T3/T4/Unknown	191 (63%)	129 (62%)	
N Stage			0.15
N0	164 (54%)	99 (48%)	
N1/NX	138 (46%)	108 (52%)	
≥80% of Protocol-Specified Concurrent Chemo			0.53
No	23 (8%)	19 (9%)	
Yes	279 (92%)	188 (91%)	
Trial			0.21
NRG/RTOG 0436	170 (56%)	117 (57%)	
NRG/RTOG 8501	76 (25%)	41 (20%)	
NRG/RTOG 9405	56 (19%)	49 (24%)	

Data are n (%) unless otherwise indicated.

Abbreviations: RT, radiation therapy; IQR, interquartile range; min, minimum; max, maximum; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group

<sup>a</sup>p-value from Chi-square/Fisher's Exact Test

**eTable 4: RT Duration ≤45 days vs >45 Days, Controlling for NRG Oncology Trial**

Endpoint	Variable	Comparison	n	Events	HR (95% CI)	p-value <sup>a</sup>
OS	RT Duration	≤ 45 days	446	354	1 (ref)	..
		> 45 days	63	55	1.32 (0.99-1.76)	0.05
	Trial	NRG/RTOG 0436	287	206	1 (ref)	..
		NRG/RTOG 8501	117	110	1.07 (0.84-1.36)	0.61
		NRG/RTOG 9405	105	93	0.91 (0.71-1.18)	0.49
DFS	RT Duration	≤ 45 days	446	386	1 (ref)	..
		> 45 days	63	59	1.41 (1.07-1.86)	0.01
	Trial	NRG/RTOG 0436	287	239	1 (ref)	..
		NRG/RTOG 8501	117	110	0.84 (0.66-1.06)	0.14
		NRG/RTOG 9405	105	96	0.89 (0.70-1.14)	0.37
LRF	RT Duration	≤ 45 days	446	247	1 (ref)	..
		> 45 days	63	41	1.38 (0.99-1.90)	0.05
	Trial	NRG/RTOG 0436	287	157	1 (ref)	..
		NRG/RTOG 8501	117	66	1.03 (0.79-1.35)	0.83
		NRG/RTOG 9405	105	65	1.22 (0.92-1.61)	0.16
DF	RT Duration	≤ 45 days	446	195	1 (ref)	..
		> 45 days	63	24	0.87 (0.56-1.35)	0.54
	Trial	NRG/RTOG 0436	287	132	1 (ref)	..
		NRG/RTOG 8501	117	43	0.70 (0.50-0.98)	0.04
		NRG/RTOG 9405	105	44	0.84 (0.60-1.19)	0.33

Abbreviations: OS, overall survival; DFS, disease-free survival; LRF, local-regional failure; DF, distant failure; HR, hazard ratio; CI, confidence interval; ref, reference level; RT, radiation therapy; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group  
<sup>a</sup>p-value from the Cox proportional hazards model (OS/DFS) or the Fine-Gray regression model (LRF/DF).

**eTable 5: RT Duration ≤45 days vs >45 Days in Patients with Squamous Cell Carcinoma Histology (n=292)**

	OS		DFS		LRF		DF	
	3y-% (95% CI)	6y-% (95% CI)	3y-% (95% CI)	6y-% (95% CI)	3y-% (95% CI)	6y-% (95% CI)	3y-% (95% CI)	6y-% (95% CI)
≤ 45 days (n=256)	39 (33,45)	23 (17,29)	30 (24,35)	19 (14,24)	52 (45,58)	54 (47,60)	35 (30,41)	37 (31,43)
> 45 days (n=36)	22 (10,37)	16 (6,30)	14 (5,27)	11 (4,24)	68 (49,81)	68 (49,81)	25 (12,40)	28 (14,43)
p-value	0.08 <sup>a</sup>		0.03 <sup>a</sup>		0.04 <sup>b</sup>		0.29 <sup>b</sup>	

Abbreviations: OS, overall survival; DFS, disease-free survival; LRF, local-regional failure; DF, distant failure; y, year; CI, confidence interval

<sup>a</sup>p-value from log-rank test

<sup>b</sup>p-value from Gray's test

**eTable 6: RT Duration ≤45 days vs >45 Days in Patients with Adenocarcinoma Histology (n=217)**

	OS		DFS		LRF		DF	
	3y-% (95% CI)	6y-% (95% CI)	3y-% (95% CI)	6y-% (95% CI)	3y-% (95% CI)	6y-% (95% CI)	3y-% (95% CI)	6y-% (95% CI)
≤ 45 days (n=190)	29 (22,35)	14 (7,23)	15 (11,21)	7 (3,15)	57 (50,64)	58 (51,65)	50 (43,57)	55 (47,62)
> 45 days (n=27)	17 (6,34)	9 (1,28)	7 (1,21)	7 (1,21)	63 (41,79)	63 (41,79)	52 (31,69)	52 (31,69)
p-value	0.42 <sup>a</sup>		0.45 <sup>a</sup>		0.51 <sup>b</sup>		0.98 <sup>b</sup>	

Abbreviations: OS, overall survival; DFS, disease-free survival; LRF, local-regional failure; DF, distant failure; y, year; CI, confidence interval

<sup>a</sup>p-value from log-rank test

<sup>b</sup>p-value from Gray's test

**eTable 7. RT Duration (Continuous), Controlling for NRG Oncology Trial**

Endpoint	Variable	Comparison	n	Events	HR (95% CI)	p-value <sup>a</sup>
OS	RT Duration	(continuous; unit increase=7 days)	509	409	1.10 (0.98-1.23)	0.10
	Trial	NRG/RTOG 0436	287	206	1 (ref)	..
		NRG/RTOG 8501	117	110	1.08 (0.85-1.38)	0.53
		NRG/RTOG 9405	105	93	0.92 (0.71-1.19)	0.52
DFS	RT Duration	(continuous; unit increase=7 days)	509	445	1.17 (1.04-1.32)	0.009
	Trial	NRG/RTOG 0436	287	239	1 (ref)	..
		NRG/RTOG 8501	117	110	0.87 (0.69-1.10)	0.25
		NRG/RTOG 9405	105	96	0.90 (0.71-1.16)	0.42
LRF	RT Duration	(continuous; unit increase=7 days)	509	288	1.17 (1.04 -1.31)	0.01
	Trial	NRG/RTOG 0436	287	157	1 (ref)	..
		NRG/RTOG 8501	117	66	1.06 (0.81-1.39)	0.66
		NRG/RTOG 9405	105	65	1.22 (0.93-1.62)	0.15
DF	RT Duration	(continuous; unit increase=7 days)	509	219	0.88 (0.74-1.05)	0.15
	Trial	NRG/RTOG 0436	287	132	1 (ref)	..
		NRG/RTOG 8501	117	43	0.68 (0.48-0.95)	0.02
		NRG/RTOG 9405	105	44	0.84 (0.60-1.18)	0.32

Abbreviations: OS, overall survival; DFS, disease-free survival; LRF, local-regional failure; DF, distant failure; HR, hazard ratio; CI, confidence interval; ref, reference level; RT, radiation therapy; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group  
<sup>a</sup>p-value from the Cox proportional hazards model (OS/DFS) or the Fine-Gray regression model (LRF/DF).



**eTable 8: RT Duration ≤39 days vs >39 Days, Controlling for NRG Oncology Trial**

Endpoint	Variable	Comparison	n	Events	HR (95% CI)	p-value <sup>a</sup>
OS	RT Duration	≤ 39 days	271	215	1 (ref)	..
		> 39 days	238	194	1.07 (0.88-1.30)	0.51
Trial		NRG/RTOG 0436	287	206	1 (ref)	..
		NRG/RTOG 8501	117	110	1.08 (0.84-1.37)	0.56
		NRG/RTOG 9405	105	93	0.92 (0.71-1.18)	0.50
DFS	RT Duration	≤ 39 days	271	231	1 (ref)	..
		> 39 days	238	214	1.21 (1.00-1.46)	0.05
Trial		NRG/RTOG 0436	287	239	1 (ref)	..
		NRG/RTOG 8501	117	110	0.84 (0.67-1.07)	0.16
		NRG/RTOG 9405	105	96	0.89 (0.70-1.14)	0.35
LRF	RT Duration	≤ 39 days	271	139	1 (ref)	..
		> 39 days	238	149	1.37 (1.10-1.71)	0.004
Trial		NRG/RTOG 0436	287	157	1 (ref)	..
		NRG/RTOG 8501	117	66	1.04 (0.80-1.36)	0.77
		NRG/RTOG 9405	105	65	1.20 (0.91-1.59)	0.19
DF	RT Duration	≤ 39 days	271	124	1 (ref)	..
		> 39 days	238	95	0.85 (0.65-1.12)	0.25
Trial		NRG/RTOG 0436	287	132	1 (ref)	..
		NRG/RTOG 8501	117	43	0.69 (0.49-0.97)	0.03
		NRG/RTOG 9405	105	44	0.86 (0.61-1.21)	0.37

Abbreviations: OS, overall survival; DFS, disease-free survival; LRF, local-regional failure; DF, distant failure; HR, hazard ratio; CI, confidence interval; ref, reference level; RT, radiation therapy; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group  
<sup>a</sup>p-value from the Cox proportional hazards model (OS/DFS) or the Fine-Gray regression model (LRF/DF).

**eTable 9: Multivariable Models: RT Duration (≤ 39 days vs. > 39 days) (n=509)**

Variables <sup>a</sup>	OS (deaths = 409)		DFS (failures = 445)		LRF (failures = 288)		DF (failures = 219)	
	HR (95% CI)	p-value <sup>b</sup>	HR (95% CI)	p-value <sup>b</sup>	HR (95% CI)	p-value <sup>b</sup>	HR (95% CI)	p-value <sup>b</sup>
RT Duration								
≤ 39 days	1 (ref)	..	1 (ref)	..	1 (ref)	..	1 (ref)	..
> 39 days	1.04 (0.85-1.26)	0.70	1.18 (0.98-1.43)	0.08	1.32 (1.06-1.65)	0.01	0.83 (0.64-1.09)	0.19
Trial								
NRG/RTOG 0436	1 (ref)	..	1 (ref)	..	1 (ref)	..	1 (ref)	..
NRG/RTOG 8501	1.11 (0.84-1.45)	0.46	1.06 (0.80-1.40)	0.70	1.20 (0.90-1.61)	0.22	0.78 (0.53-1.14)	0.20
NRG/RTOG 9405	0.96 (0.73-1.25)	0.74	1.07 (0.81-1.41)	0.62	1.32 (0.99-1.77)	0.06	1.01 (0.70-1.47)	0.95
Age (continuous; unit increase=10)	---	---	---	---	0.86 (0.77-0.97)	0.01	0.84 (0.73-0.97)	0.02
Sex								
Female	1 (ref)	..	---	---	---	---	---	---
Male	1.49 (1.13-1.95)	0.004	---	---	---	---	---	---
Race								
Other	---	---	---	---	---	---	---	---
White	---	---	---	---	---	---	---	---
Zubrod								
0	1 (ref)	..	1 (ref)	..	1 (ref)	..	---	---
1 or 2	1.26 (1.04-1.53)	0.02	1.27 (1.05-1.54)	0.01	1.30 (1.04-1.61)	0.02	---	---
Tumor size (cm)								
< 5	1 (ref)	..	1 (ref)	..	---	---	1 (ref)	..
≥ 5	1.44 (1.16-1.79)	0.001	1.32 (1.08-1.62)	0.008	---	---	1.35 (1.01-1.79)	0.04
N Stage								
N0	1 (ref)	..	1 (ref)	..	1 (ref)	..	---	---
NX/N1	1.37 (1.10-1.70)	0.005	1.37 (1.11-1.69)	0.004	1.37 (1.08-1.74)	0.01	---	---
Histology								
Adenocarcinoma	---	---	1 (ref)	..	---	---	1 (ref)	..
Squamous	---	---	0.72 (0.58-0.89)	0.003	---	---	0.60 (0.45-0.81)	<0.001
≥80% of Protocol-Specified Concurrent Chemo								
No	---	---	1 (ref)	..	---	---	---	---
Yes	---	---	0.66 (0.47-0.92)	0.01	---	---	---	---

Abbreviations: OS, overall survival; DFS, disease-free survival; LRF, local-regional failure; DF, distant failure; HR, hazard ratio; CI, confidence interval; ref, reference level; RT, radiation therapy; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group; Chemo, chemotherapy

<sup>a</sup>RT duration and NRG Oncology trial are included in each model and other variables are included if p-value <0.05.  
<sup>b</sup>p-value from the Cox proportional hazards model (OS/DFS) or the Fine-Gray regression model (LRF/DF).

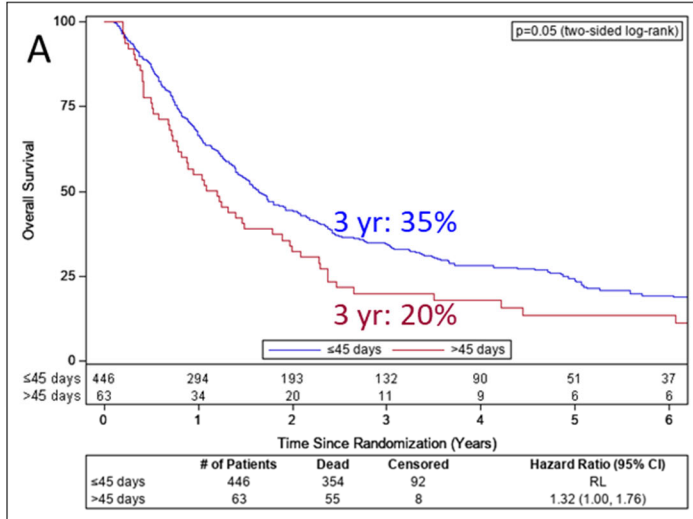
**eTable 10: RT Interruptions, Controlling for NRG Oncology Trial**

Endpoint	Variable	Comparison	n	Events	HR (95% CI)	p-value <sup>a</sup>
OS	RT Interruptions	No	302	240	1 (ref)	..
		Yes	207	169	1.15 (0.94-1.40)	0.16
	Trial	NRG/RTOG 0436	287	206	1 (ref)	..
		NRG/RTOG 8501	117	110	1.08 (0.84-1.37)	0.55
		NRG/RTOG 9405	105	93	0.91 (0.71-1.18)	0.47
DFS	RT Interruptions	No	302	259	1 (ref)	..
		Yes	207	186	1.19 (0.99 -1.44)	0.07
	Trial	NRG/RTOG 0436	287	239	1 (ref)	..
		NRG/RTOG 8501	117	110	0.85 (0.67-1.07)	0.16
		NRG/RTOG 9405	105	96	0.89 (0.69-1.14)	0.34
LRF	RT Interruptions	No	302	162	1 (ref)	..
		Yes	207	126	1.22 (0.98-1.52)	0.08
	Trial	NRG/RTOG 0436	287	157	1 (ref)	..
		NRG/RTOG 8501	117	66	1.04 (0.79-1.36)	0.79
		NRG/RTOG 9405	105	65	1.21 (0.92-1.60)	0.17
DF	RT Interruptions	No	302	128	1 (ref)	..
		Yes	207	91	1.04 (0.80-1.37)	0.75
	Trial	NRG/RTOG 0436	287	132	1 (ref)	..
		NRG/RTOG 8501	117	43	0.70 (0.50-0.98)	0.04
		NRG/RTOG 9405	105	44	0.84 (0.60-1.18)	0.32

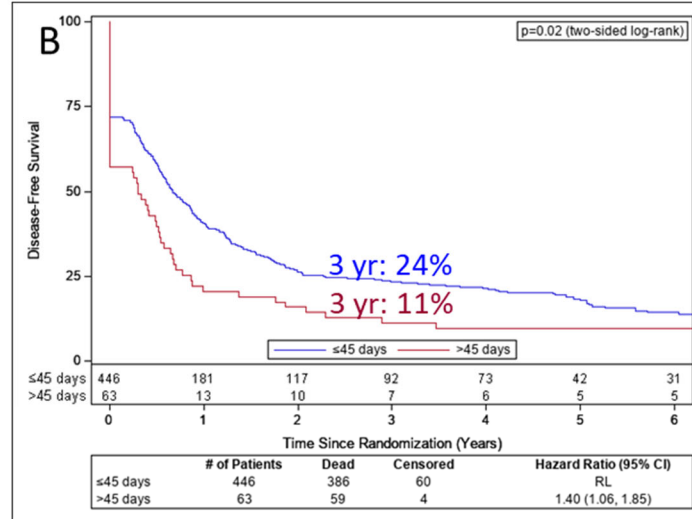
Abbreviations: OS, overall survival; DFS, disease-free survival; LRF, local-regional failure; DF, distant failure; HR, hazard ratio; CI, confidence interval; ref, reference level; RT, radiation therapy; NRG/RTOG, NRG Oncology/Radiation Therapy Oncology Group  
<sup>a</sup>p-value from the Cox proportional hazards model (OS/DFS) or the Fine-Gray regression model (LRF/DF).

**eFigure 1. Outcomes for RT duration dichotomized by XTile cutpoint**

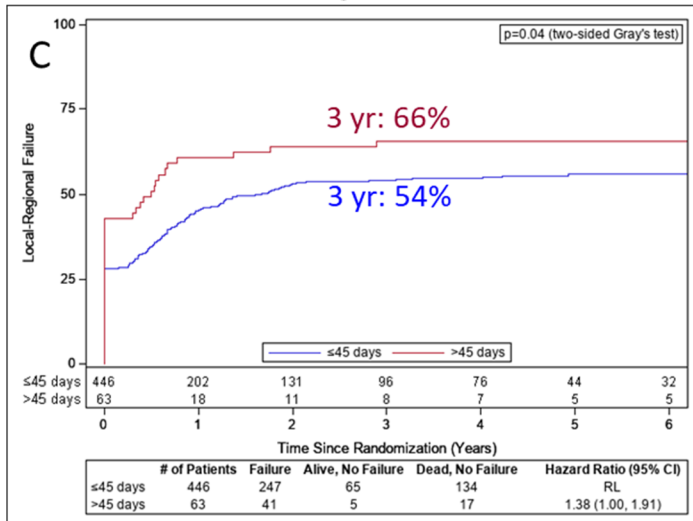
**Overall Survival**



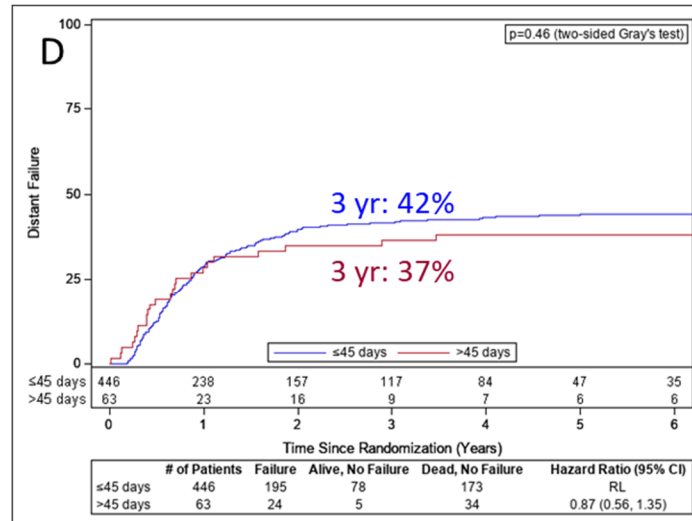
**Disease-Free Survival**



**Local-Regional Failure**

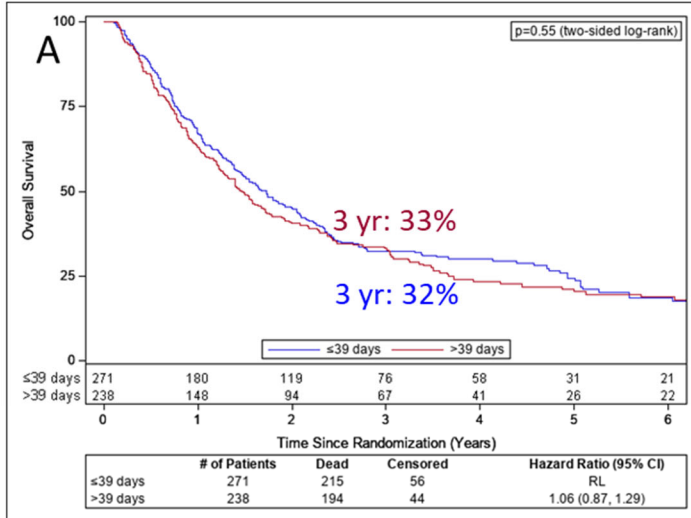


**Distant Failure**

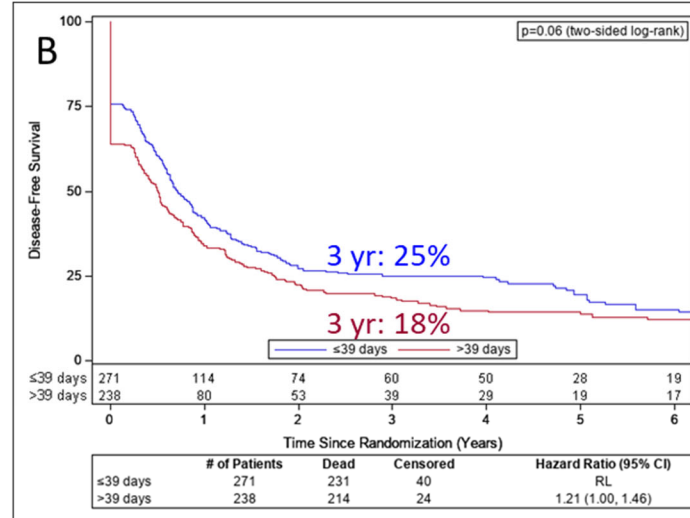


**eFigure 2. Outcomes for RT duration dichotomized by median**

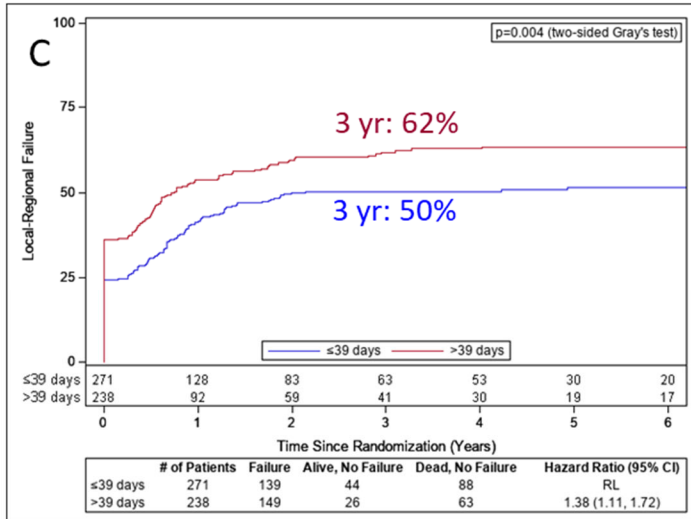
**Overall Survival**



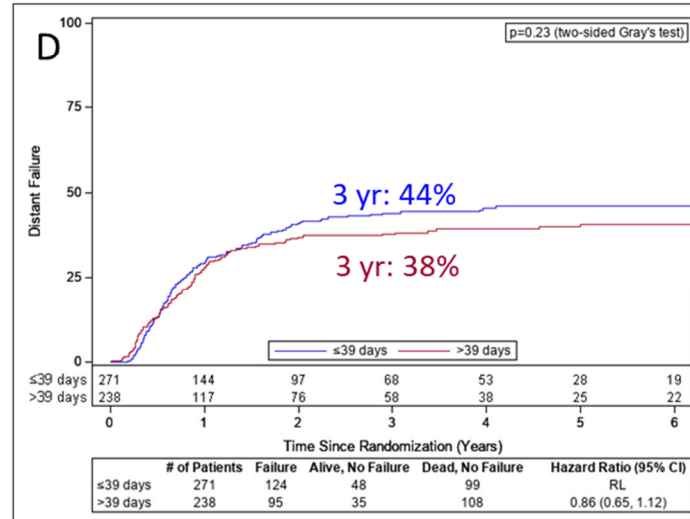
**Disease-Free Survival**



**Local-Regional Failure**

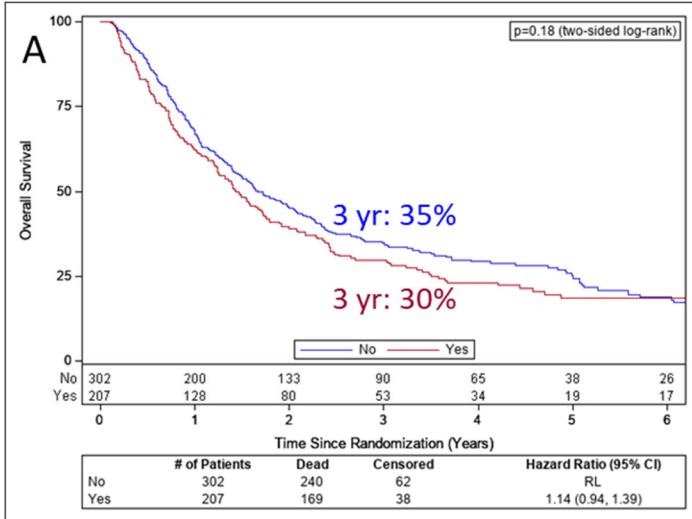


**Distant Failure**

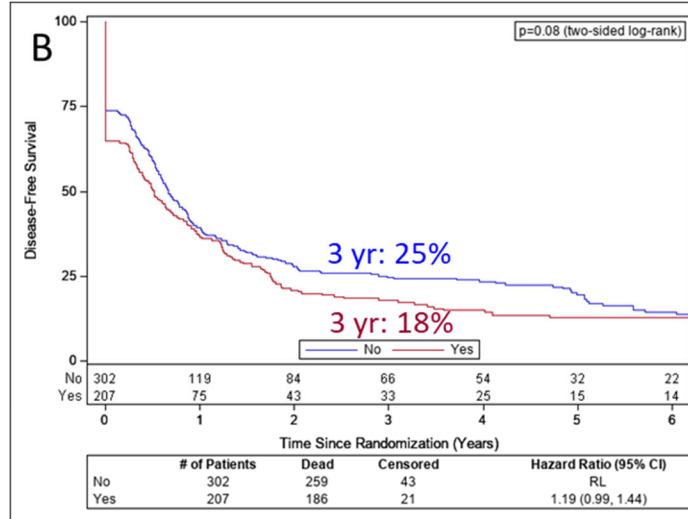


**eFigure 3. Outcomes for RT interruption**

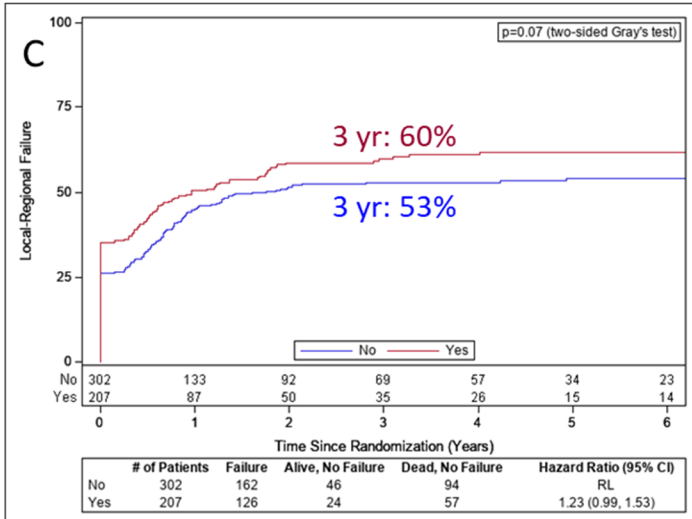
**Overall Survival**



**Disease-Free Survival**



**Local-Regional Failure**



**Distant Failure**

