

Supplementary Online Content

Kehl KL, Greenwald S, Chamoun NG, Manberg PJ, Schrag D. Association between first-line immune checkpoint inhibition and survival for Medicare-insured patients with advanced non-small cell lung cancer. *JAMA Netw Open*. 2021;4(5):e2111113. doi:10.1001/jamanetworkopen.2021.11113

eTable 1. Propensity Score Model: Pembrolizumab vs Platinum/Pemetrexed

eTable 2. Propensity Score Model: Pembrolizumab vs Platinum/Taxane

eTable 3. Propensity Score Model: Platinum/Pemetrexed/Pembrolizumab vs Platinum/Pemetrexed

eTable 4. Propensity Score-Stratified Associations Between Treatment Regimen and Overall Survival by Age Group

eFigure 1. Targeted Therapy Exclusion Cohort Derivation (Sensitivity Analysis)

eFigure 2. Kaplan-Meier Overall Survival Curves by Quintile of Baseline Prediction of 1-Year Mortality at Time of Initial Treatment

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

eTable 1. Propensity Score Model: Pembrolizumab vs Platinum/Pemetrexed

	Odds Ratio for Treatment with pembrolizumab vs. platinum/pemetrexed	
Characteristics	Odd Ratio Mean (95% CI*)	p
Age at the index lung cancer event		
66-69	Reference	
70-79	1.32 (1.16-1.50)	<0.001
80-89	2.86 (2.44-3.35)	<0.001
Sex		
Male	Reference	
Female	1.23 (1.11-1.37)	<0.001
Race/Ethnicity		
White non-Hispanic	Reference	
Black non-Hispanic	0.83 (0.67-1.04)	0.10
Hispanic	0.86 (0.44-1.69)	0.67
Other	0.99 (0.77-1.28)	0.93
Medicaid enrollment		
No	Reference	
Yes	1.15 (1.01-1.32)	0.04
Median household income in census tract of residence (quintile)		
Lowest 20%	Reference	
20-40%	0.93 (0.78-1.12)	0.46
40-60%	0.88 (0.74-1.05)	0.16
60-80%	0.94 (0.78-1.14)	0.55
Highest 20%	0.84 (0.69-1.02)	0.08
Urban-rural status of patient's county		
Large metro	Reference	
Metro	1.18 (0.95-1.47)	0.13
Urban	1.12 (0.98-1.27)	0.09
Less urban	1.39 (0.97-1.98)	0.07
Rural	1.03 (0.82-1.30)	0.78
% of adults with college in patient's zip code of residence (quintile)		
Lowest 20%	Reference	
20-40%	1.15 (0.95-1.39)	0.15
40-60%	1.17 (0.96-1.43)	0.11
60-80%	1.23 (0.99-1.51)	0.06
Highest 20%	1.37 (1.10-1.70)	0.005
Risk stratification index (RSI) at baseline		
Lowest 20%	Reference	
20-40%	1.33 (1.12,1.59)	0.002
40-60%	1.57 (1.32,1.87)	<0.001

60-80%	1.86 (1.57,2.21)	<0.001
Highest 20%	2.60 (2.19,3.08)	<0.001
Date of initial systematic lung cancer treatment		
2016_Q1	Reference	
2016_Q2	**	**
2016_Q3	**	**
2016_Q4	**	**
2017_Q1	37.44 (18.32-76.52)	<0.001
2017_Q2	55.83 (27.30-114.19)	<0.001
2017_Q3	53.19 (25.97-108.95)	<0.001
2017_Q4	50.48 (24.65-103.37)	<0.001
2018_Q1	64.65 (31.60-132.26)	<0.001
2018_Q2	62.60 (30.53-128.36)	<0.001
2018_Q3	79.97 (38.93-164.29)	<0.001
2018_Q4	N/A	

** Cell information suppressed consistent with Centers for Medicare and Medicaid Services (CMS) cell size suppression policy.

N/A: Too few subjects from Q4 2018 were included in the cohort to provide stable estimates.

eTable 2. Propensity Score Model: Pembrolizumab vs Platinum/Taxane

	Odds Ratio for Treatment with pembrolizumab vs. platinum/taxane	
Characteristics	Odd Ratio Mean (95% CI*)	P
Age at the index lung cancer event		
66-69	Reference	
70-79	1.01 (0.90-1.14)	0.81
80-89	1.60 (1.40-1.83)	<0.001
Sex		
Male	Reference	
Female	1.66 (1.52-1.82)	<0.001
Race/Ethnicity		
White non-Hispanic	Reference	
Black non-Hispanic	0.85 (0.71-1.03)	0.09
Hispanic	1.43 (0.78-2.61)	0.25
Other	1.38 (1.09-1.73)	0.006
Medicaid enrollment		
No	Reference	
Yes	0.74 (0.66-0.83)	<0.001
Median household income in census tract of residence (quintile)		
Lowest 20%	Reference	
20-40%	0.97 (0.84-1.13)	0.71
40-60%	1.06 (0.91-1.23)	0.47
60-80%	1.13 (0.97-1.33)	0.11
Highest 20%	1.32 (1.11-1.56)	0.001
Urban-rural status of patient's county		
Large metro	Reference	
Metro	0.95 (0.79-1.14)	0.57
Urban	0.97 (0.86-1.08)	0.55
Less urban	1.03 (0.77-1.38)	0.83
Rural	0.87 (0.72-1.06)	0.16
% of adults with college in patient's zip code of residence (quintile)		
Lowest 20%	Reference	
20-40%	1.18 (1.01-1.37)	0.04
40-60%	1.27 (1.08-1.50)	0.004
60-80%	1.34 (1.12-1.60)	0.001
Highest 20%	1.73 (1.44-2.09)	<0.001
Risk stratification index (RSI) at baseline		
Lowest 20%	Reference	
20-40%	1.33 (1.13-1.55)	<0.001

40-60%	2.01 (1.72-2.34)	<0.001
60-80%	2.60 (2.24-3.03)	<0.001
Highest 20%	4.19 (3.60-4.87)	<0.001
Date of initial systematic lung cancer treatment		
2016_Q1	Reference	
2016_Q2	**	**
2016_Q3	**	**
2016_Q4	**	**
2017_Q1	34.32 (16.86-69.87)	<0.001
2017_Q2	39.53 (19.43-80.41)	<0.001
2017_Q3	35.55 (17.46-72.36)	<0.001
2017_Q4	40.41 (19.84-82.31)	<0.001
2018_Q1	49.98 (24.57-101.70)	<0.001
2018_Q2	39.04 (19.18-79.49)	<0.001
2018_Q3	43.01 (21.13-87.57)	<0.001
2018_Q4	N/A	

** Cell information suppressed, consistent with Centers for Medicare and Medicaid Services (CMS) cell size suppression policy.

N/A: Too few subjects from Q4 2018 were included in the cohort to provide stable estimates.

eTable 3. Propensity Score Model: Platinum/Pemetrexed/Pembrolizumab vs Platinum/Pemetrexed

	Odds Ratio for Treatment with pembrolizumab/platinum/pemetrexed vs. platinum/pemetrexed	
Characteristics	Odd Ratio Mean (95% CI*)	P
Age at the index lung cancer event		
66-69	Reference	
70-79	1.06 (0.90-1.23)	0.50
80-89	0.85 (0.68-1.07)	0.16
Sex		
Male	Reference	
Female	1.00 (0.87-1.14)	0.95
Race/ethnicity		
White non-Hispanic	Reference	
Black non-Hispanic	0.78 (0.59-1.04)	0.10
Hispanic	0.68 (0.25-1.83)	0.45
Other	0.82 (0.59-1.15)	0.26
Medicaid enrollment		
No	Reference	
Yes	0.92 (0.77-1.11)	0.40
Median household income in census tract of residence (quintile)		
Lowest 20%	Reference	
20-40%	1.02 (0.81-1.29)	0.86
40-60%	0.95 (0.75-1.20)	0.64
60-80%	0.99 (0.77-1.27)	0.95
Highest 20%	0.84 (0.64-1.09)	0.18
Urban-rural status of patient's county		
Large Metro	Reference	
Metro	1.15 (0.87-1.51)	0.34
Urban	0.93 (0.78-1.11)	0.41
Less Urban	1.20 (0.78-1.85)	0.41
Rural	0.98 (0.73-1.32)	0.91
% of adults with college in patient's zip code of residence (quintile)		
Lowest 20%	Reference	
20-40%	1.04 (0.82-1.33)	0.74
40-60%	0.98 (0.76-1.27)	0.90
60-80%	1.12 (0.85-1.47)	0.41
Highest 20%	1.17 (0.88-1.55)	0.29
Risk stratification index (RSI) at baseline		
Lowest 20%	Reference	
20-40%	1.27 (1.02-1.58)	0.03

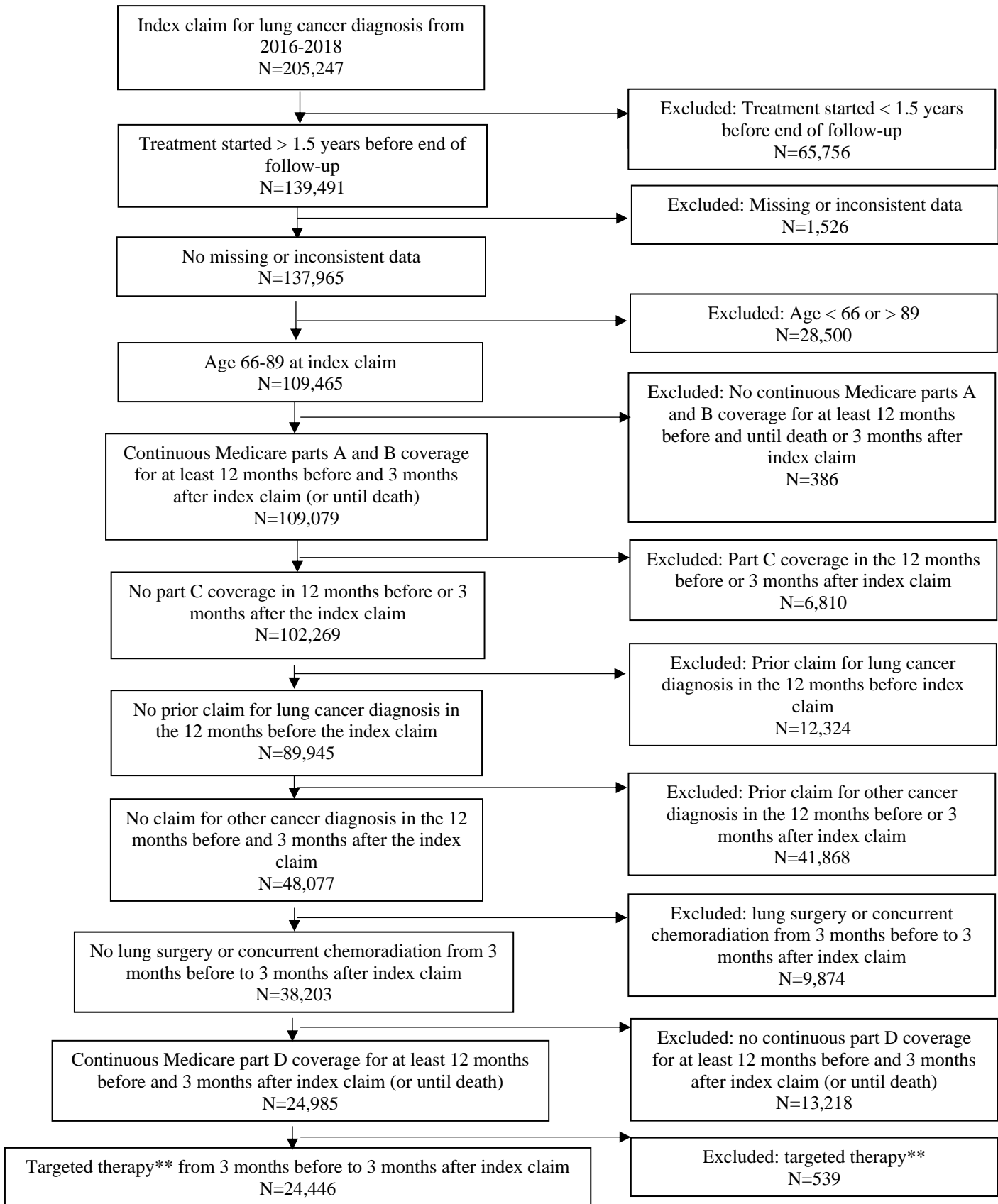
40-60%	1.44 (1.15-1.78)	0.001
60-80%	1.55 (1.24-1.93)	<0.001
Highest 20%	1.75 (1.40-2.19)	<0.001
Date of initial systematic lung cancer treatment		
2016	Reference	
2017	656.55 (92.19-4675.71)	<0.001
2018	N/A	

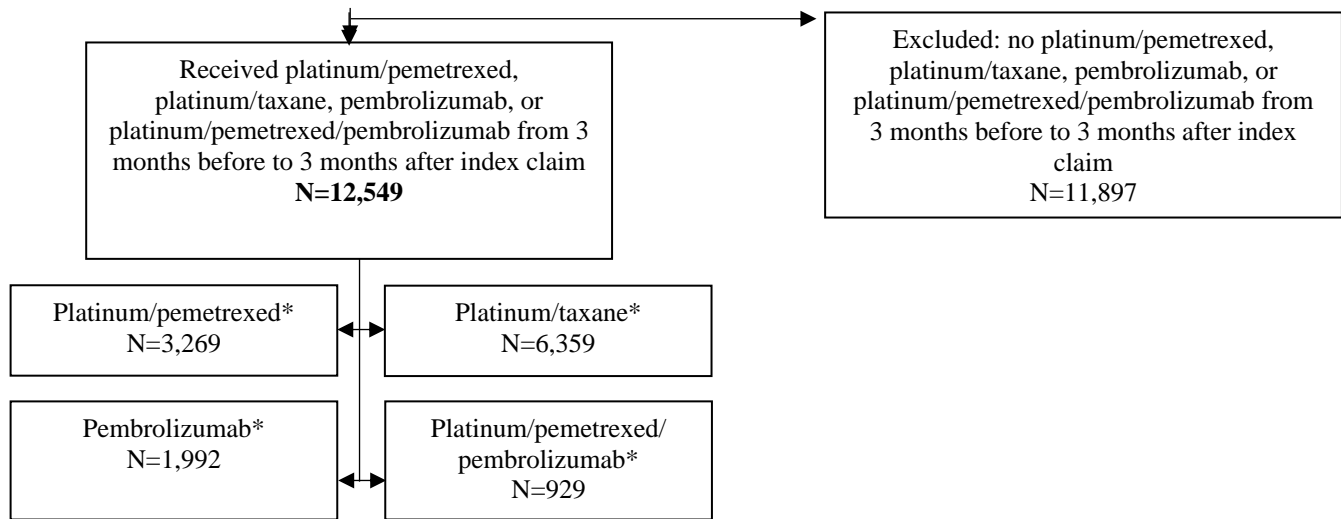
N/A: Too few subjects from Q4 2018 were included in the cohort to provide stable estimates.

eTable 4. Propensity Score-Stratified Associations Between Treatment Regimen and Overall Survival by Age Group

Comparison	Age Cohort	N	Propensity score-adjusted results			p
			RMST* (95% CI): Reference group	RMST* (95% CI): Pembrolizumab group	RMST* difference (95% CI)	
Pembrolizumab vs platinum/pemetrexed	66-69	2,133	10.8 (10.4-11.2)	10.7 (9.9-11.5)	-0.1 (-0.8, 0.6)	0.80
	70-79	4,492	11.1 (10.8-11.3)	10.9 (10.3-11.4)	-0.2 (-0.7, 0.2)	0.33
	80-89	1,613	10.7 (10.0-11.4)	10.2 (9.2-11.2)	-0.5 (-1.3, 0.3)	0.21
Pembrolizumab vs platinum/taxane	66-69	3,025	11.5 (11.2-11.8)	11.2 (10.5-11.9)	-0.3 (-1.0, 0.3)	0.30
	70-79	7,251	11.7 (11.5-11.9)	10.8 (10.4-11.3)	-0.9 (-1.3, -0.5)	<0.001
	80-89	2,669	11.2 (10.9-11.6)	10.5 (9.7-11.2)	-0.8 (-1.4, -0.2)	0.009
Pembrolizumab/platinum/pemetrexed vs platinum/pemetrexed	66-69	1,938	11.4 (11.0-11.8)	12.3 (11.4-13.1)	1.0 (0.1, 1.8)	0.02
	70-79	3,761	11.4 (11.1-11.7)	11.7 (11.1-12.3)	0.3 (-0.2, 0.9)	0.24
	80-89	885	10.5 (9.9-11.0)	10.5 (9.2-11.9)	0.1 (-1.1, 1.3)	0.90

eFigure 1. Targeted Therapy Exclusion Cohort Derivation (Sensitivity Analysis)



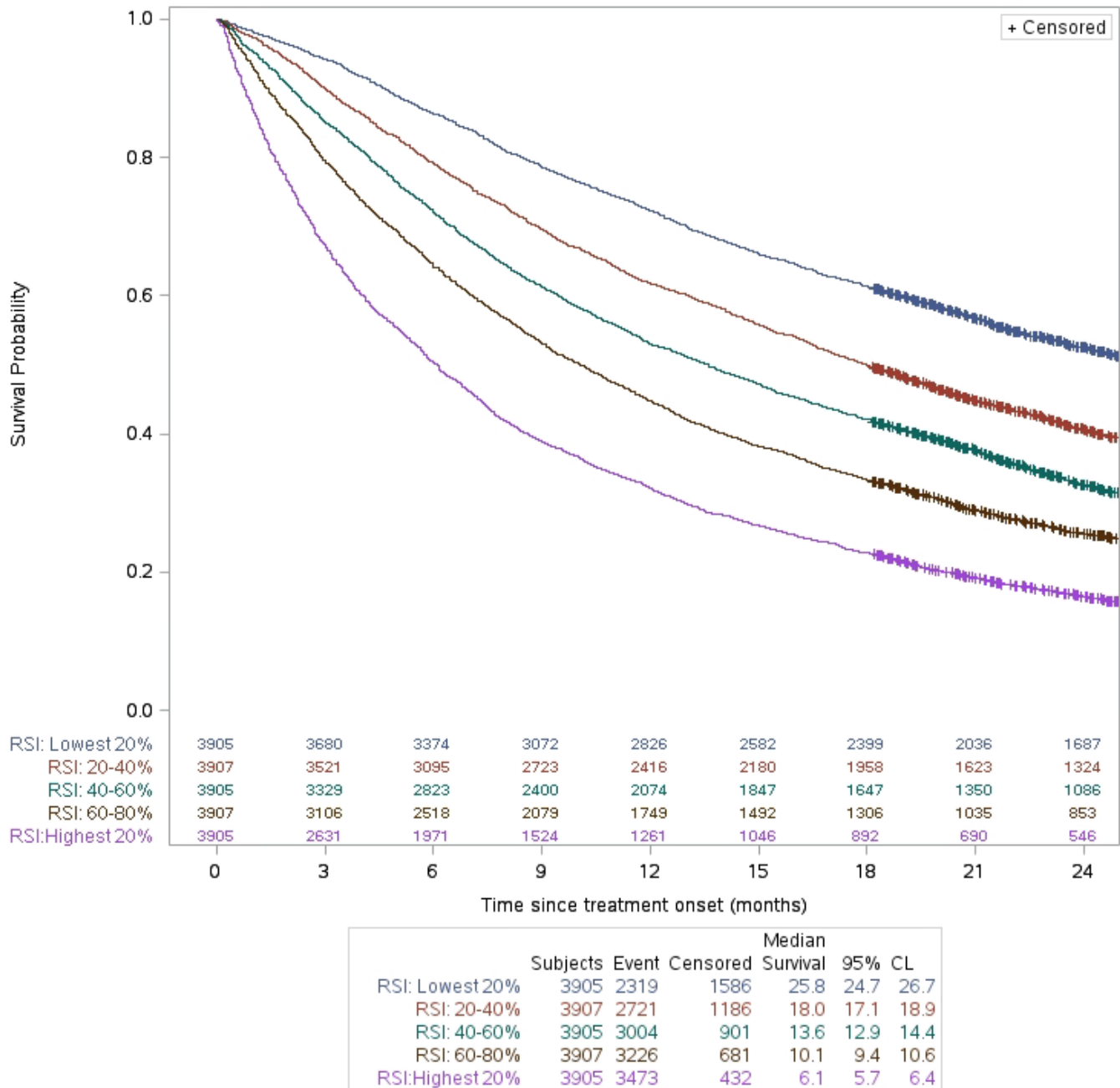


Legend to Figure S1:

* A treatment regimen was defined as any combination of chemotherapy drugs, the first dose of each of which was administered within 21 days of the first dose of the first drug given in the regimen. Platinum was defined as cisplatin or carboplatin; taxane was defined as paclitaxel, nab-paclitaxel, or docetaxel. Co-administration of bevacizumab was not considered to define a distinct regimen.

** Targeted therapy was defined as any of the following drugs: Gefitinib, erlotinib, afatinib, dacomitinib, osimertinib, crizotinib, ceritinib, brigatinib, alectinib, lorlatinib, dabrafenib, trametinib.

eFigure 2. Kaplan-Meier Overall Survival Curves by Quintile of Baseline Prediction of 1-Year Mortality at Time of Initial Treatment



Legend to Figure S2: RSI, Risk stratification index