

## Supplementary Online Content

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

**eTable 1.** Comparison of Demographic and Clinical Factors Between Patients Included in vs Excluded From the Biomarker Cohort

Characteristics <sup>a</sup>	Included (N = 1,494)	Excluded (N = 1,032)
Age (years)	61.3 (54.0-68.8)	61.4 (53.1-68.6)
Sex		
Male	828 (55.4)	564 (54.7)
Female	666 (44.6)	468 (45.3)
Race <sup>b</sup>		
Asian	52 (3.5)	55 (5.3)
Black	163 (10.9)	156 (15.1)
Others	49 (3.3)	52 (5.0)
White	1,230 (82.3)	769 (74.5)
Ethnicity		
Hispanic	82 (5.5)	109 (10.6)
Non-Hispanic	1,412 (94.5)	923 (89.4)
ECOG performance status <sup>c</sup>		
0	1,076 (72.0)	721 (69.9)
1-2	418 (28.0)	311 (30.1)
Bowel wall invasion by T stage <sup>d</sup>		
T1-T2	290 (19.6)	158 (15.6)
T3	984 (66.4)	690 (68.1)
T4	209 (14.1)	166 (16.4)
Missing	11	18
Nodal stage <sup>e</sup>		
N1	1,090 (73.5)	750 (74.0)
N2	392 (26.5)	263 (26.0)
Missing	12	19
Tumor location		
Left-sided	716 (48.5)	456 (44.66)
Right-sided	754 (51.0)	561 (54.95)

Multiple	7 (0.5)	4 (0.39)
Missing	17	11
BMI (kg/m <sup>2</sup> )	28.0 (24.6-32.2)	27.8 (24.2-31.6)

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group.

<sup>a</sup> Continuous variables were presented as median (interquartile), and categorical variables as number (percentage). Percentages may not add up to 100% because of rounding.

<sup>b</sup> Participants who did not self-identify as Asian, Black or White were classified as others for race.

<sup>c</sup> ECOG performance status: 0, fully active, able to carry on all predisease performance without restriction; 1, restricted in physically strenuous activity but ambulatory and able to carry out light work; 2, ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours.

<sup>d</sup> Bowel wall invasion: T1, tumor has grown into the submucosa; T2, growth into the muscularis propria; T3, grown through the muscularis propria and into the subserosa; and T4, grown into the surface of the visceral peritoneum or into or has attached to other organs or structures.

<sup>e</sup> Nodal stage: N1, 1 to 3 lymph nodes tested positive for cancer; N2, 4 or more positive lymph nodes.

**eTable 2.** Demographic and Clinical Characteristics of Colon Cancer Patients by Quintiles of Inflammatory Biomarkers

	IL-6					
Characteristics <sup>a</sup>	Q1 (N = 298)	Q2 (N = 300)	Q3 (N = 300)	Q4 (N = 299)	Q5 (N = 297)	P-value
Age (years)	58.7 (50.7-66.7)	60.2 (53.2-68.0)	60.9 (53.9-68.0)	64.5 (56.5-70.9)	63.7 (55.8-70.6)	<0.001
Sex						0.27
Male	149 (50.0)	176 (58.7)	169 (56.3)	170 (56.9)	164 (55.2)	
Female	149 (50.0)	124 (41.3)	131 (43.7)	129 (43.1)	133 (44.8)	
Race <sup>b</sup>						0.07
Asian	19 (6.4)	11 (3.7)	12 (4.0)	5 (1.7)	5 (1.7)	
Black	24 (8.1)	30 (10.0)	35 (11.7)	37 (12.4)	37 (12.5)	
Others	9 (3.0)	14 (4.7)	8 (2.7)	11 (3.7)	7 (2.4)	
White	246 (82.6)	245 (81.7)	245 (81.7)	246 (82.3)	248 (83.5)	
Ethnicity						0.02
Hispanic	19 (6.4)	27 (9.0)	12 (4.0)	12 (4.0)	12 (4.0)	
Non-Hispanic	279 (93.6)	273 (91.0)	288 (96.0)	287 (96.0)	285 (96.0)	
ECOG performance status <sup>c</sup>						<0.001
0	231 (77.5)	231 (77.0)	215 (71.7)	211 (70.6)	188 (63.3)	
1-2	67 (22.5)	69 (23.0)	85 (28.3)	88 (29.4)	109 (36.7)	
Bowel wall invasion by T stage <sup>d</sup>						0.24
T1-T2	68 (23.1)	59 (19.7)	56 (18.7)	53 (17.9)	54 (18.5)	
T3	196 (66.4)	201 (67.2)	193 (64.3)	206 (69.4)	188 (64.4)	
T4	31 (10.5)	39 (13.0)	51 (17.0)	38 (12.8)	50 (17.1)	
Missing	3	1	0	2	5	
Nodal stage <sup>e</sup>						0.17
N1	218 (74.1)	224 (74.9)	233 (77.7)	205 (69.0)	210 (71.9)	
N2	76 (25.9)	75 (25.1)	67 (22.3)	92 (31.0)	82 (28.1)	
Missing	4	1	0	2	5	
Tumor location <sup>f</sup>						0.06
Left-sided	158 (53.7)	153 (52.0)	139 (46.5)	138 (46.5)	128 (43.7)	
Right-sided	136 (46.3)	138 (46.9)	160 (53.5)	156 (52.5)	164 (56.0)	

Multiple	0 (0)	3 (1.0)	0 (0)	3 (1.0)	1 (0.3)	
Missing	4	6	1	2	4	
BMI (kg/m <sup>2</sup> )	26.0 (23.0-28.8)	27.2 (24.2-30.8)	28.6 (25.1-32.6)	29.4 (25.5-34.0)	30.2 (36.0-36.1)	<0.001
Time between surgery and blood collection <sup>g</sup> (months)	1.5 (1.2-1.8)	1.6 (1.3-1.9)	1.6 (1.3-1.9)	1.6 (1.3-1.9)	1.5 (1.2-1.8)	0.34
Blood sample storage time (months)	58.5 (44.7-73.0)	59.4 (44.9-70.9)	57.2 (44.1-69.6)	56.7 (44.5-71.4)	56.9 (43.8-70.5)	0.94
			sTNF-αR2			
	Q1 (N = 297)	Q2 (N = 299)	Q3 (N = 300)	Q4 (N = 299)	Q5 (N = 299)	P-value
Age (years)	56.0 (50.5-62.3)	58.7 (52.2-66.2)	60.9 (54.2-68.1)	64.5 (57.1-70.8)	66.9 (59.7-73.6)	<0.001
Sex						0.85
Male	157 (52.9)	166 (55.5)	171 (57.0)	164 (54.8)	170 (56.9)	
Female	140 (47.1)	133 (44.5)	129 (43.0)	135 (45.2)	129 (43.1)	
Race <sup>b</sup>						<0.001
Asian	22 (7.4)	10 (3.3)	10 (3.3)	6 (2.0)	4 (1.3)	
Black	39 (13.1)	36 (12.0)	34 (11.3)	29 (9.7)	25 (8.4)	
Others	17 (5.7)	8 (2.7)	11 (3.7)	9 (3.0)	4 (1.3)	
White	219 (73.7)	245 (81.9)	245 (81.7)	255 (85.3)	266 (89.0)	
Ethnicity						0.002
Hispanic	27 (9.1)	14 (4.7)	17 (5.7)	19 (6.4)	5 (1.7)	
Non-Hispanic	270 (90.9)	285 (95.3)	283 (94.3)	280 (93.6)	294 (98.3)	
ECOG performance status <sup>c</sup>						<0.001
0	237 (79.8)	241 (80.6)	222 (74.0)	202 (67.6)	174 (58.2)	
1-2	60 (20.2)	58 (19.4)	78 (26.0)	97 (32.4)	125 (41.8)	
Bowel wall invasion by T stage <sup>d</sup>						<0.001
T1-T2	73 (24.8)	67 (22.6)	61 (20.5)	50 (16.9)	39 (13.1)	
T3	199 (67.5)	183 (61.6)	197 (66.3)	197 (66.6)	209 (69.8)	
T4	23 (7.8)	47 (15.8)	39 (13.1)	49 (16.6)	51 (17.1)	
Missing	2	2	3	3	1	
Nodal stage <sup>e</sup>						0.88
N1	220 (74.1)	216 (72.2)	227 (75.7)	222 (74.2)	217 (72.6)	

N2	77 (25.9)	83 (27.8)	73 (24.3)	77 (25.8)	82 (27.4)	
Missing	3	2	3	3	1	
Tumor location <sup>f</sup>						0.001
Left-sided	166 (56.5)	152 (51.0)	144 (48.8)	142 (48.1)	112 (38.0)	
Right-sided	128 (43.5)	146 (49.0)	149 (50.5)	150 (50.9)	181 (61.4)	
Multiple	0 (0)	0 (0)	2 (0.7)	3 (1.0)	2 (0.7)	
Missing	3	1	5	4	4	
BMI (kg/m <sup>2</sup> )	26.4 (23.3-29.6)	28.1 (24.1-31.7)	27.8 (24.8-31.9)	28.7 (25.1-33.1)	29.3 (25.7-36.4)	<0.001
Time between surgery and blood collection <sup>g</sup> (months)	1.6 (1.3-1.9)	1.5 (1.2-1.8)	1.6 (1.3-2.0)	1.6 (1.2-1.8)	1.5 (1.2-1.9)	0.07
Blood sample storage time (months)	57.5 (42.7-69.4)	58.5 (43.6-69.7)	55.3 (44.4-70.6)	59.7 (48.0-72.6)	57.4 (47.4-72.4)	0.16
			hsCRP			
	Q1 (N = 300)	Q2 (N = 299)	Q3 (N = 299)	Q4 (N = 299)	Q5 (N = 297)	<i>P</i> -value
Age (years)	60.4 (53.6-68.6)	62.5 (54.6-70.0)	61.5 (54.3-68.7)	61.4 (53.9-68.3)	60.6 (53.9-68.4)	0.45
Sex						0.09
Male	162 (54.0)	176 (58.9)	178 (59.5)	165 (55.2)	147 (49.5)	
Female	138 (46.0)	123 (41.1)	121 (40.5)	134 (44.8)	150 (50.5)	
Race <sup>b</sup>						<0.001
Asian	22 (7.3)	8 (2.7)	9 (3.0)	6 (2.0)	7 (2.4)	
Black	20 (6.7)	26 (8.7)	36 (12.0)	35 (11.7)	46 (15.5)	
Others	14 (4.7)	6 (2.0)	13 (4.4)	9 (3.0)	7 (2.4)	
White	244 (81.3)	259 (86.6)	241 (80.6)	249 (83.3)	237 (79.8)	
Ethnicity						0.92
Hispanic	17 (5.7)	17 (5.7)	18 (6.0)	17 (5.7)	13 (4.4)	
Non-Hispanic	283 (94.3)	282 (94.3)	281 (94.0)	282 (94.3)	284 (95.6)	
ECOG performance status <sup>c</sup>						0.01
0	232 (77.3)	225 (75.3)	217 (72.5)	206 (68.9)	196 (66.0)	
1-2	68 (22.7)	74 (24.7)	82 (27.4)	93 (31.1)	101 (34.0)	
Bowel wall invasion by T stage <sup>d</sup>						0.22
T1-T2	63 (21.1)	60 (20.2)	69 (23.2)	48 (16.1)	50 (17.1)	

T3	186 (62.4)	201 (67.7)	185 (62.3)	206 (68.9)	206 (70.6)	
T4	49 (16.4)	36 (12.1)	43 (14.5)	45 (15.1)	36 (12.3)	
Missing	2	2	2	0	5	
Nodal stage <sup>e</sup>						0.27
N1	230 (77.4)	220 (74.1)	207 (69.7)	215 (71.9)	218 (74.7)	
N2	67 (22.6)	77 (25.9)	90 (30.3)	84 (28.1)	74 (25.3)	
Missing	3	2	2	0	5	
Tumor location <sup>f</sup>						0.08
Left-sided	162 (54.9)	150 (50.7)	144 (48.16)	131 (44.0)	129 (43.9)	
Right-sided	132 (45.8)	145 (49.0)	148 (50.3)	164 (55.0)	165 (56.1)	
Multiple	1 (0.3)	1 (0.3)	2 (0.7)	3 (1.0)	0 (0)	
Missing	5	3	5	1	3	
BMI (kg/m <sup>2</sup> )	25.7 (22.4-28.9)	27.0 (23.5-29.8)	28.0 (25.3-32.0)	29.3 (26.0-34.4)	30.8 (26.3-36.7)	<0.001
Time between surgery and blood collection <sup>g</sup> (months)	1.6 (1.3-1.9)	1.6 (1.3-1.9)	1.5 (1.3-1.9)	1.6 (1.3-1.9)	1.5 (1.2-1.8)	0.29
Blood sample storage time (months)	59.3 (44.5-71.0)	57.2 (46.1-68.4)	57.1 (44.7-71.4)	55.5 (42.9-73.3)	58.2 (44.7-72.6)	0.94

Abbreviations: BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; Q1, quintile 1; Q2, quintile 2; Q3, quintile 3; Q4, quintile 4; Q5, quintile 5.

<sup>a</sup> Continuous variables were presented as median (interquartile), and categorical variables as number (percentage). Percentages may not add up to 100% because of rounding.

<sup>b</sup> Participants who did not self-identify as Asian, Black, or White were classified as others for race.

<sup>c</sup> ECOG performance status: 0, fully active, able to carry on all predisease performance without restriction; 1, restricted in physically strenuous activity but ambulatory and able to carry out light work; 2, ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours.

<sup>d</sup> Bowel wall invasion: T1, tumor has grown into the submucosa; T2, growth into the muscularis propria; T3, grown through the muscularis propria and into the subserosa; and T4, grown into the surface of the visceral peritoneum or into or has attached to other organs or structures.

<sup>e</sup> Nodal stage: N1, 1 to 3 lymph nodes tested positive for cancer; N2, 4 or more positive lymph nodes.

<sup>f</sup> Given small sample size for tumor located at multiple sites, chi-squared tests were performed for left- vs. right-sided.

<sup>g</sup> Number of missing for time between surgery and blood collection: 13

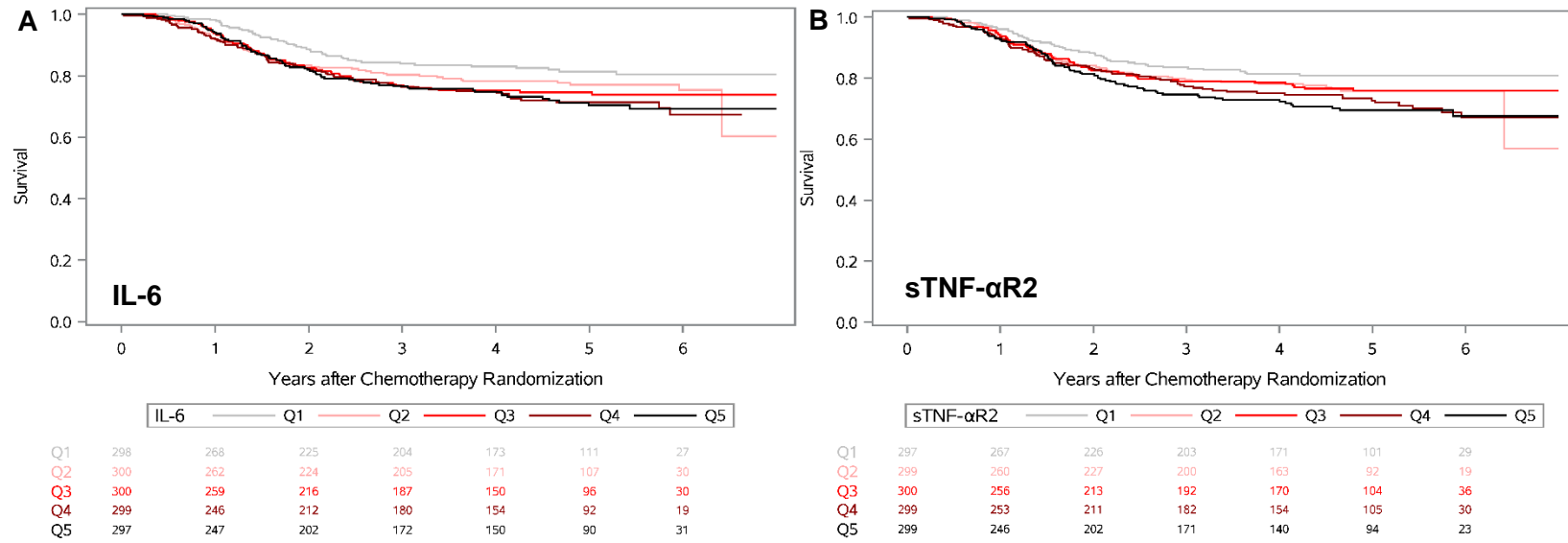
**eTable 3.** Five-Year Survival From the Kaplan-Meier Estimator by Quintiles of Inflammatory Biomarkers

Disease-free Survival, % (95% CI)			
Quintiles	IL-6	sTNF- $\alpha$ R2	hsCRP
Q1	79.2 (73.6-83.7)	80.5 (75.2-84.9)	79.5 (74.2-83.9)
Q2	76.1 (70.5-80.8)	73.5 (67.6-78.6)	73.2 (67.3-78.2)
Q3	70.0 (64.0-75.3)	72.0 (66.0-77.1)	67.4 (61.2-72.8)
Q4	67.0 (60.7-72.6)	69.6 (63.4-75.0)	71.9 (65.7-77.1)
Q5	65.9 (59.4-71.6)	62.9 (56.5-68.6)	66.6 (60.1-72.2)
Recurrence-free Survival			
Quintiles	IL-6	sTNF- $\alpha$ R2	hsCRP
Q1	81.3 (75.8-85.7)	92.8 (88.9-95.3)	89.9 (85.6-93.0)
Q2	77.0 (71.4-81.6)	86.2 (81.4-89.8)	87.8 (83.2-91.2)
Q3	74.5 (68.7-79.4)	85.2 (80.3-89.0)	81.0 (75.7-85.2)
Q4	71.3 (65.2-76.6)	83.6 (78.5-87.5)	84.5 (79.5-88.3)
Q5	70.3 (63.9-75.9)	76.0 (70.4-80.7)	80.6 (75.3-84.9)
Overall Survival			
Quintiles	IL-6	sTNF- $\alpha$ R2	hsCRP
Q1	81.3 (75.8-85.7)	80.8 (75.4-85.1)	81.0 (75.7-85.3)
Q2	77.0 (71.4-81.6)	75.8 (70.0-80.6)	76.5 (70.7-81.2)
Q3	74.5 (68.7-79.4)	75.8 (70.0-80.7)	70.2 (64.1-75.4)
Q4	71.3 (65.2-76.6)	72.6 (66.5-77.8)	75.6 (69.6-80.5)
Q5	70.3 (63.9-75.9)	69.3 (63.0-74.8)	71.5 (65.1-76.8)

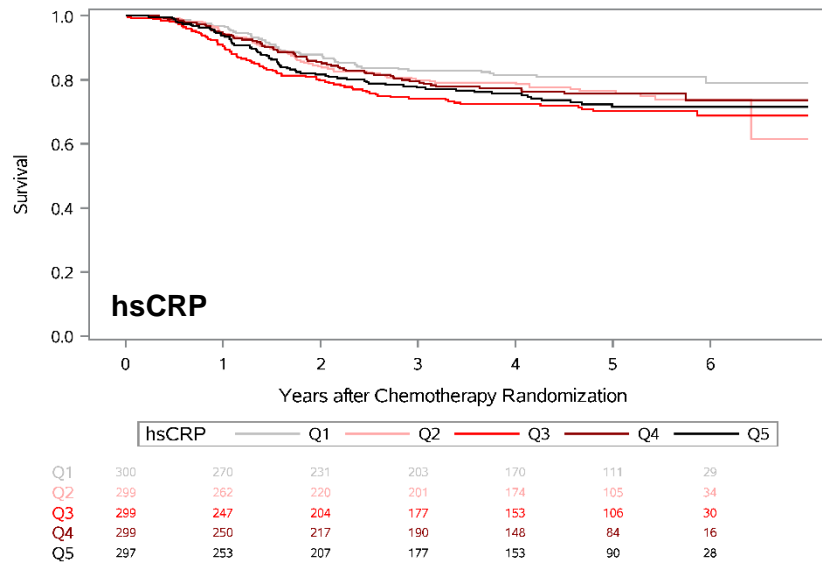
Abbreviations: Q1, quintile 1; Q2, quintile 2; Q3, quintile 3; Q4, quintile 4; Q5, quintile 5.



**eFigure 1.** Kaplan-Meier Estimates for Recurrence-Free Survival by Quintiles of Inflammatory Biomarkers Among Patients With Stage III Colon Cancer



**C**



Abbreviations: Q1, quintile 1; Q2, quintile 2; Q3, quintile 3; Q4, quintile 4; Q5, quintile 5.

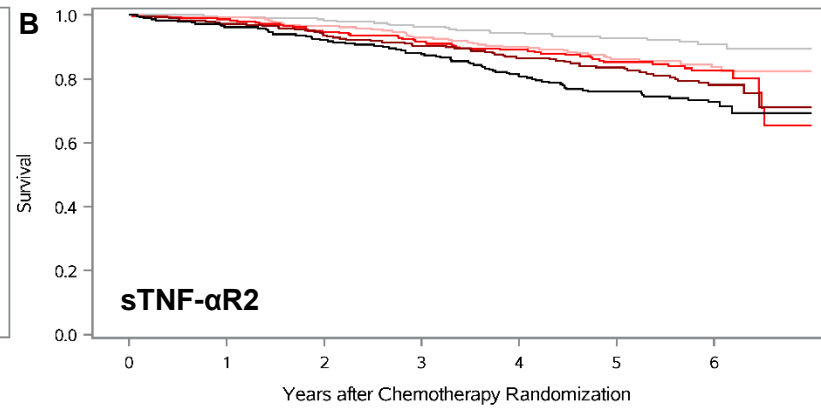
Recurrence-free survival by quintiles of IL-6 (eFigure 1A), sTNF- $\alpha$ R2 (eFigure 1B), hsCRP (eFigure 1C). *P*-values for each inflammatory biomarker were calculated using the log-rank test: IL-6 (*P*-value = 0.05), sTNF- $\alpha$ R2 (*P*-value = 0.04), and hsCRP (*P*-value = 0.06).

**eFigure 2.** Kaplan-Meier Estimates for Overall Survival by Quintiles of Inflammatory Biomarkers Among Patients With Stage III Colon Cancer



IL-6	Q1	Q2	Q3	Q4	Q5
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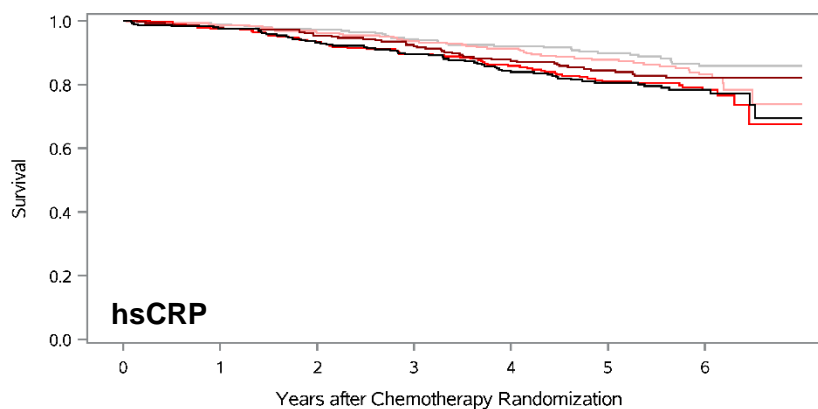
Q1	298	286	269	259	243	189	99
Q2	300	285	266	256	241	183	108
Q3	300	282	268	250	234	176	94
Q4	299	273	252	238	227	175	97
Q5	297	274	253	230	215	164	98



sTNF- $\alpha$ R2	Q1	Q2	Q3	Q4	Q5
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Q1	297	289	270	253	243	184	109
Q2	299	284	271	256	242	179	102
Q3	300	280	260	247	233	177	91
Q4	299	279	257	240	224	177	100
Q5	299	268	250	237	218	170	94

**C**



hsCRP	Q1	Q2	Q3	Q4	Q5		
Q1	300	287	271	255	240	186	107
Q2	299	284	265	253	243	196	112
Q3	299	278	257	240	228	178	90
Q4	299	277	260	244	227	164	87
Q5	297	274	255	241	222	163	100

Abbreviations: Q1, quintile 1; Q2, quintile 2; Q3, quintile 3; Q4, quintile 4; Q5, quintile 5.

Overall survival by quintiles of IL-6 (eFigure 2A), sTNF- $\alpha$ R2 (eFigure 2B), hsCRP (eFigure 2C). *P*-values for each inflammatory biomarker were calculated using the log-rank test: IL-6 (*P*-value = 0.008), sTNF- $\alpha$ R2 (*P*-value <0.001), and hsCRP (*P*-value = 0.02).

**eTable 4.** Unadjusted Associations of Inflammatory Biomarkers With Survival Among Patients With Stage III Colon Cancer

Survival	Q1	Q2	Q3	Q4	Q5	<i>P</i> for Trend
Disease-free Survival						
IL-6	1.00	1.16 (0.82-1.65)	1.42 (1.01-1.99)	1.65 (1.19-2.30)	1.70 (1.22-2.36)	<0.001
sTNF- $\alpha$ R2	1.00	1.39 (0.97-1.98)	1.50 (1.05-2.13)	1.75 (1.24-2.47)	2.10 (1.50-2.94)	<0.001
hsCRP	1.00	1.39 (0.99-1.95)	1.69 (1.21-2.36)	1.38 (0.98-1.95)	1.64 (1.18-2.30)	0.003
Recurrence-free Survival						
IL-6	1.00	1.32 (0.91-1.92)	1.47 (1.02-2.12)	1.65 (1.15-2.37)	1.62 (1.13-2.33)	0.02
sTNF- $\alpha$ R2	1.00	1.30 (0.90-1.89)	1.30 (0.90-1.89)	1.57 (1.10-2.25)	1.68 (1.18-2.40)	0.006
hsCRP	1.00	1.29 (0.90-1.87)	1.68 (1.18-2.39)	1.30 (0.90-1.89)	1.48 (1.03-2.12)	0.03
Overall survival						
IL-6	1.00	1.53 (0.97-2.40)	1.65 (1.06-2.59)	1.90 (1.22-2.94)	2.16 (1.40-3.33)	<0.001
sTNF- $\alpha$ R2	1.00	1.86 (1.12-3.09)	2.20 (1.34-3.62)	2.59 (1.60-4.21)	3.49 (2.18-5.57)	<0.001
hsCRP	1.00	1.34 (0.86-2.10)	1.88 (1.23-2.86)	1.43 (0.92-2.24)	1.86 (1.22-2.84)	<0.001

Abbreviations: Q1, quintile 1; Q2, quintile 2; Q3, quintile 3; Q4, quintile 4; Q5, quintile 5.

**eTable 5.** Sensitivity Analysis of Incorporating Diet and Lifestyle Factors for Adjusted Associations of Inflammatory Biomarkers With Survival Among Patients With Stage III Colon Cancer

Survival	Q1	Q2	Q3	Q4	Q5	<i>P</i> for Trend
Disease-free Survival						
IL-6	1.00	1.06 (0.75-1.52)	1.33 (0.94-1.89)	1.40 (0.99-1.99)	1.42 (1.00-2.01)	0.04
sTNF- $\alpha$ R2	1.00	1.18 (0.82-1.70)	1.37 (0.95-1.97)	1.54 (1.07-2.22)	1.67 (1.15-2.42)	0.003
hsCRP	1.00	1.29 (0.91-1.83)	1.59 (1.13-2.24)	1.22 (0.85-1.75)	1.56 (1.10-2.22)	0.02
Recurrence-free Survival						
IL-6	1.00	1.25 (0.86-1.84)	1.44 (0.99-2.11)	1.51 (1.03-2.22)	1.45 (0.99-2.14)	0.14
sTNF- $\alpha$ R2	1.00	1.11 (0.76-1.62)	1.23 (0.84-1.80)	1.45 (0.99-2.13)	1.45 (0.98-2.16)	0.07
hsCRP	1.00	1.23 (0.85-1.79)	1.61 (1.11-2.32)	1.18 (0.80-1.74)	1.49 (1.02-2.17)	0.06
Overall Survival						
IL-6	1.00	1.37 (0.86-2.18)	1.58 (0.99-2.51)	1.45 (0.91-2.31)	1.63 (1.03-2.59)	0.04
sTNF- $\alpha$ R2	1.00	1.53 (0.91-2.57)	1.84 (1.10-3.06)	1.91 (1.14-3.20)	2.22 (1.33-3.72)	0.004
hsCRP	1.00	1.25 (0.79-1.96)	1.71 (1.10-2.64)	1.17 (0.74-1.86)	1.64 (1.05-2.56)	0.007

Abbreviations: Q1, quintile 1; Q2, quintile 2; Q3, quintile 3; Q4, quintile 4; Q5, quintile 5.

<sup>a</sup> Adjusted for age (years), sex (male or female), race (White, Black, Asian, Others), ethnicity (Hispanic or Non-Hispanic), ECOG performance status (0 or 1-2), T stage (T1-T2, T3, T4), N stage (N or N2), tumor location (left-sided, right-sided, multiple), BMI (kg/m<sup>2</sup>; <18.5, 18.5-24.9, 25.0-29.9, 30+), time between surgery and blood draw (months), blood sample storage time (months), diet quality (measured by Western dietary pattern score), smoking (never, past, current), low dose aspirin usage (yes or no), physical activity (metabolic equivalent task hours per week [MET-hours/week]; 0-2.9, 3-8.9, 9-17.9, 18+), and treatment arm (celecoxib or placebo).