

Table 1. Characteristics of subjects after excluding subjects with missing values[#]

	NMIBC (n = 601)	MIBC (n = 77)	All (n = 678)
Age			
Median (Q1, Q3)	66 (57,71)	67 (59,72)	66 (58,71)
Sex			
Male	455 (75.7%)	56 (72.7%)	511 (75.4%)
Female	146 (24.3%)	21 (27.3%)	167 (24.6%)
Tumor grade			
Grade 1	289 (48.1%)	2 (2.6%)	291 (42.9%)
Grade 2	161 (26.8%)	11 (14.3%)	172 (25.4%)
Grade 3	125 (20.8%)	29 (37.7%)	154 (22.7%)
Grade 4	26 (4.3%)	35 (45.5%)	61 (9.0%)
Smoking status			
Never	103 (17.1%)	16 (20.8%)	119 (17.6%)
Ever	498 (82.9%)	61 (79.2%)	559 (82.4%)
BCG: Immunotherapy			
No	512 (85.2%)	72 (93.5%)	587 (86.6%)
Yes	89 (14.8%)	2 (6.5%)	91 (13.4%)
NLR			
Median (Q1, Q3)	2.08 (1.46, 3.09)	2.51 (1.66,4.13)	2.11 (1.48,3.18)
10-year dead status			
Alive	423 (70.4%)	27 (35.1%)	450 (66.4%)
Deceased	178 (29.6%)	50 (64.9%)	228 (33.6%)
10-year Recurrence-free status*			
No	230 (38.3%)	19 (24.7%)	249 (36.7%)
Yes	371 (61.7%)	58 (75.3%)	429 (63.3%)

[#]: Exclude subjects with missing values in muscle-invasive status, pathology reviewing status, tumor grade, smoking status

*: whether patient with tumor recurrence or deceased within 10 years.

Table 2. Cox proportional hazards models of immune cell proportions and bladder cancer patient outcomes

	10-year overall survival				10-year recurrence-free survival			
	Univariate model		Multivariable [§] model		Univariate model		Multivariable [#] model	
	HR (95% CI)	P value	HR	FDR	HR (95% CI)	P value	HR	FDR
NLR	1.35 (1.27-1.43)	5.9E-23	1.25	6.8E-10	1.12 (1.06-1.17)	1.8E-5	1.11	0.003
Memory B cell	0.80 (0.70-0.92)	1.3E-3	0.89	0.09	0.91 (0.84-1.00)	0.047	0.96	0.38
Naïve B cell	0.84 (0.78-0.91)	3.2E-6	0.91	0.02	0.98 (0.93-1.02)	0.30		
Memory CD4T cell	0.93 (0.90-0.95)	2.2E-8	0.97	0.02	0.97 (0.96-0.99)	3.0E-3	0.98	0.06
Naïve CD4T cell	0.88 (0.84-0.93)	5.3E-6	0.96	0.14	0.96 (0.92-0.99)	6.5E-3	0.98	0.27
Memory CD8T cell	0.96 (0.94-0.99)	3.3E-3	0.94	5.1E-5	0.99 (0.97-1.00)	0.11		
Naïve CD8T cell	0.83 (0.75-0.91)	1.1E-4	1.06	0.29	0.92 (0.86-0.98)	9.8E-3	0.99	0.78
Monocyte	1.04 (1.00-1.09)	0.06			1.05 (1.02-1.08)	3.2E-3	1.04	0.06
Neutrophil	1.05 (1.04-1.06)	1.0E-14	1.04	5.6E-7	1.01 (1.00-1.02)	5.7E-3	1.01	0.08
Regulatory T cell	1.00 (0.89-1.14)	0.95			1.02 (0.94-1.12)	0.60		
NK cell	0.92 (0.87-0.98)	6.2E-3	0.91	0.008	0.98 (0.94-1.02)	0.35		
Basophil	1.03 (0.94-1.14)	0.50			1.02 (0.95-1.09)	0.66		
Eosinophil	0.99 (0.93-1.06)	0.75			1.02 (0.97-1.07)	0.47		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

§: The model controlling for age, sex, stratified muscle-invasive status, tumor grade, smoking status, BCG treatment status, age acceleration.

#: The model controlling for age, stratified sex, stratified muscle-invasive status, tumor grade, smoking status, stratified BCG treatment status.

Supplemental Table 1. Cox proportional hazards models of immune cell proportions and NMIBC patient outcomes

	10-year overall survival				10-year recurrence-free survival			
	Univariate model		Multivariable [§] model		Univariate model		Multivariable [#] model	
	HR (95% CI)	P value	HR	FDR	HR (95% CI)	P value	HR	FDR
NLR	1.39 (1.30-1.48)	5.7E-21	1.32	1.3E-11	1.11 (1.05-1.18)	1.6E-4	1.10	0.01
Memory B cell	0.81 (0.69-0.94)	5.9E-3	0.89	0.13	0.92 (0.84-1.01)	0.08		
Naïve B cell	0.84 (0.77-0.91)	2.4E-5	0.90	0.02	0.98 (0.94-1.03)	0.45		
Memory CD4T cell	0.93 (0.90-0.95)	4.9E-7	0.96	0.02	0.97 (0.96-0.99)	5.3E-3	0.98	0.08
Naïve CD4T cell	0.85 (0.80-0.91)	1.1E-6	0.92	0.03	0.95 (0.92-0.99)	6.4E-3	0.97	0.20
Memory CD8T cell	0.96 (0.93-0.99)	3.9E-3	0.94	1.3E-4	0.99 (0.97-1.01)	0.29		
Naïve CD8T cell	0.82 (0.73-0.91)	2.3E-4	1.05	0.45	0.92 (0.86-0.99)	0.02	0.99	0.79
Monocyte	1.04 (0.99-1.10)	0.09			1.04 (1.01-1.08)	0.01	1.03	0.11
Neutrophil	1.06 (1.04-1.07)	1.9E-14	1.04	1.1E-7	1.01 (1.00-1.02)	0.01	1.01	0.11
Regulatory T cell	0.95 (0.81-1.11)	0.49			1.02 (0.93-1.12)	0.67		
NK cell	0.90 (0.84-0.96)	2.3E-3	0.89	1.5E-3	0.97 (0.93-1.02)	0.20		
Basophil	1.02 (0.91-1.14)	0.73			1.02 (0.94-1.10)	0.64		
Eosinophil	1.01 (0.94-1.09)	0.81			1.02 (0.97-1.07)	0.47		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

§: The model controlling for age, sex, tumor grade, smoking status, BCG treatment status, age acceleration.

#: The model controlling for age, stratified sex, tumor grade, smoking status, stratified BCG treatment status.

Supplemental Table 3. Cox proportional hazards models of immune cell proportions and MIBC patient outcomes

	10-year overall survival		10-year recurrence-free survival	
	Univariate model		Univariate model	
	HR (95% CI)	P value	HR (95% CI)	P value
NLR	1.12 (0.99-1.27)	0.08	1.11 (0.98-1.25)	0.10
Memory B cell	0.90 (0.68-1.18)	0.43	0.89 (0.69-1.15)	0.38
Naïve B cell	0.92 (0.80-1.07)	0.28	0.96 (0.84-1.09)	0.51
Memory CD4T cell	0.97 (0.92-1.03)	0.32	0.99 (0.94-1.04)	0.63
Naïve CD4T cell	1.04 (0.94-1.15)	0.43	1.00 (0.91-1.09)	0.93
Memory CD8T cell	0.97 (0.92-1.02)	0.21	0.96 (0.91-1.01)	0.08
Naïve CD8T cell	0.99 (0.80-1.23)	0.92	0.92 (0.76-1.13)	0.44
Monocyte	1.02 (0.93-1.12)	0.64	1.08 (0.99-1.18)	0.07
Neutrophil	1.01 (0.99-1.04)	0.35	1.01 (0.99-1.03)	0.48
Regulatory T cell	1.14 (0.92-1.43)	0.24	1.02 (0.82-1.27)	0.85
NK cell	1.02 (0.92-1.14)	0.66	1.06 (0.96-1.16)	0.27
Basophil	1.04 (0.86-1.25)	0.70	0.98 (0.82-1.17)	0.84
Eosinophil	0.96 (0.85-1.09)	0.52	1.03 (0.92-1.15)	0.65

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

#: The model controlling for age, sex, tumor grade, smoking status, BCG treatment status.

Supplemental Table 3. Cox proportional hazards models of immune cell profiles and bladder cancer patient outcomes

	10-year overall survival				10-year recurrence-free survival			
	Univariate model		Multivariable [§] model		Univariate model		Multivariable [#] model	
	HR (95% CI)	P value	HR	FDR	HR (95% CI)	P value	HR	FDR
CD4T	0.94 (0.92-0.96)	6.1E-10	0.97	2.5E-3	0.98 (0.96-0.99)	6.3E-4	0.99	0.08
CD8T	0.94 (0.92-0.97)	4.4E-5	0.94	1.0E-4	0.98 (0.96-1.00)	0.02	0.98	0.04
B cell	0.84 (0.79-0.90)	3.7E-8	0.90	2.1E-3	0.97 (0.93-1.01)	0.12		
Lymphocyte	0.95 (0.93-0.96)	1.2E-15	0.96	4.0E-8	0.98 (0.98-0.99)	1.8E-4	0.99	0.04
Naïve cell	0.91 (0.89-0.94)	6.1E-9	0.96	0.02	0.97 (0.96-0.99)	0.01	1.00	0.69
NLR	1.35 (1.27-1.43)	5.9E-23	1.26	2.7E-11	1.12 (1.06-1.17)	1.8E-5	1.09	0.01
Lymph / Mono	0.89 (0.85-0.94)	4.6E-6	0.93	2.5E-3	0.96 (0.94-0.99)	1.8E-3	0.97	0.04
Bnv / Total Bcell	0.99 (0.99, 1.00)	1.5E-5	0.995	0.02	1.00 (1.00, 1.00)	0.39		
CD4T/CD8T	0.96 (0.89-1.04)	0.29			0.99 (0.94-1.04)	0.64		
CD4nv / Total CD4	0.98 (0.97, 0.99)	3.86E-5	0.99	0.08	0.99 (0.99, 1.00)	0.02	1.00	0.46
CD4nv / CD4mem	0.52 (0.34, 0.81)	0.004	0.76	0.17	0.77 (0.59, 1.01)	0.06		
CD8nv / Total CD8	1.00 (0.99, 1.00)	0.38			1.00 (0.99, 1.00)	0.42		
CD8nv / CD8mem	0.97 (0.82, 1.15)	0.73			0.98 (0.88, 1.11)	0.78		
CD8mem / Treg								
High		Referent Group				Referent Group		
Low	1.19 (0.92-1.55)	0.181			1.20 (0.99-1.45)	0.06		
Treg / Total CD4	1.01 (1.00, 1.02)	0.140			1.00 (1.00, 1.01)	0.30		
Naïve / Lymph	0.12 (0.04, 0.34)	6.8E-5	0.82	0.73	0.52 (0.25, 1.08)	0.08		

HR: hazard ratio, CI: confidence interval, NLR: neutrophil to lymphocyte ratio

Winsorization was used on the top 2% values for fitting linearity assumption.

§: The model controlling for age, sex, stratified muscle-invasive status, tumor grade, smoking status, BCG treatment status.

#: The model controlling for age, stratified sex, stratified muscle-invasive status, tumor grade, smoking status, stratified BCG treatment status.

Supplemental Table 2. Distributions of immune profiles

	NMIBC (n = 601)	MIBC (n = 77)	All (n = 678)
CD4T (%)			
Median (Q1, Q3)	11.8 (7.9, 17.4)	9.3 (4.8, 14.8)	11.7 (7.6, 17.0)
Min, Max	0.0, 49.7	0.0, 37.7	0.0, 49.7
CD8T (%)			
Median (Q1, Q3)	7.5 (4.7, 11.8)	7.3 (4.7, 9.0)	7.5 (4.7, 11.8)
Min, Max	0.0, 39.4	0.0, 29.2	0.0, 39.4
B cell (%)			
Median (Q1, Q3)	3.3 (1.7, 4.9)	2.5 (1.1, 4.1)	3.2 (1.6, 4.9)
Min, Max	0.0, 18.7	0.0, 11.9	0.0, 18.7
Lymphocyte (%)			
Median (Q1, Q3)	28.8 (21.6, 36.6)	25.1 (16.9, 33.9)	29.5 (21.0, 36.4)
Min, Max	2.7, 72.4	6.1, 60.9	2.7, 72.4
Naïve cell (%)			
Median (Q1, Q3)	5.4 (2.4, 9.7)	4.1 (0.8, 8.0)	5.2 (2.1, 9.5)
Min, Max	0.0, 32.1	0.0, 22.2	0.0, 32.1
NLR			
Median (Q1, Q3)	2.1 (1.5, 3.1)	2.5 (1.7, 4.1)	2.1 (1.5, 3.2)
Min, Max	0.2, 32.0	0.2, 13.4	0.2, 32.0
Lymphocyte / Monocyte			
Median (Q1, Q3)	3.8 (2.6, 5.8)	3.6 (2.0, 5.5)	3.8 (2.5, 5.8)
Min, Max	0.2, 2469.0	0.5, 38.7	0.2, 2469.0
B naïve / Total B cell (%)			
Median (Q1, Q3)	58.3 (28.5, 78.2)	46.8 (0.0, 87.1)	57.9 (21.8, 78.6)
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0
CD4T / CD8T			
Median (Q1, Q3)	1.6 (0.9, 2.6)	1.4 (0.5, 2.3)	1.6 (0.9, 2.5)
Min, Max	0.0, 3270.0	0.0, 136.0	0.0, 3270.0
CD4nv / Total CD4T (%)			
Median (Q1, Q3)	12.3 (0.0, 27.5)	4.9 (0.0, 24.6)	11.7 (0.0, 27.1)
Min, Max	0.0, 80.8	0.0, 63.8	0.0, 80.8
CD4T naïve / CD4T mem			
Median (Q1, Q3)	0.1 (0.0, 0.4)	0.1 (0.0, 0.4)	0.1 (0.0, 0.4)

Min, Max	0.0, 544.0	0.0, 61.0	0.0, 544.0
CD8nv / Total CD8T (%)			
Median (Q1, Q3)	16.8 (0.0, 36.3)	14.1 (0.0, 34.4)	16.6 (0.0, 36.1)
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0
CD8T naïve / CD8T mem			
Median (Q1, Q3)	0.2 (0.0, 0.6)	0.2 (0.0, 0.5)	0.2 (0.0, 0.6)
Min, Max	0.0, 690.0	0.0, 4.6	0.0, 690.0
Treg / Total CD4T (%)			
Median (Q1, Q3)	0.0 (0.0, 1.7)	0.0 (0.0, 5.1)	0.0 (0.0, 1.9)
Min, Max	0.0, 100.0	0.0, 100.0	0.0, 100.0
CD8T mem / Treg			
Median (Q1, Q3)	352.0 (17.2, 757.0)	310.0 (25.7, 603.0)	351.5 (17.4, 747.0)
Min, Max	0.0, 2481.0	0.0, 2923.0	0.0, 2923.0
Naïve / Lymphocyte			
Median (Q1, Q3)	0.2 (0.1, 0.3)	0.2 (0.0, 0.3)	0.2 (0.1, 0.3)
Min, Max	0.0, 0.6	0.0, 0.4	0.0, 0.6
