

# Molecular classification using Lund University algorithm and clinical correlations in muscle-invasive bladder cancer: Insights from a retrospective study

## SUPPLEMENTARY FILE

**Table S1. Correlation between immunohistochemically-based subtypes and clinical variables**

Variable (number of patients=347)	Luminal- like URO- NAS (%)	Luminal- like GU (%)	Basal-like (%)	NULL (%)	p-value
Sex					
M	83 (23.92)	62 (17.87)	37 (10.66)	23 (6.63)	0.074
F	47 (15.54)	34 (9.80)	38 (10.95)	23 (6.63)	
Class age					
≤60 years old	17 (4.90)	14 (4.03)	9 (2.59)	3 (0.86)	0.565
61–70 years old	35 (10.09)	17 (4.90)	15 (4.32)	7 (2.02)	
71–80 years old	43 (12.39)	24 (6.92)	21 (6.05)	20 (5.76)	
≥80 years old	50 (14.41)	26 (7.49)	30 (8.65)	16 (4.61)	
Oncologic medical history <sup>#</sup>					
No prior history	89 (25.65)	57 (16.43)	57 (16.43)	29 (8.36)	0.040*
Previous urothelial tumors	27 (7.78)	12 (3.46)	6 (1.73)	6 (1.73)	
Previous other malignancies	17 (4.90)	11 (3.17)	9 (2.59)	11 (3.17)	
Both previous urothelial tumors and other malignancies	12 (3.46)	1 (0.29)	3 (0.86)	0	
Procedure					
TURBT	50 (14.41)	30 (8.65)	20 (5.76)	13 (3.75)	0.465
Cystectomy	95 (27.38)	51 (14.70)	55 (15.85)	33 (9.51)	
Vital status					
Alive	49 (14.12)	35 (10.09)	24 (6.92)	17 (4.90)	0.310
Deceased	85 (24.50)	36 (10.37)	42 (12.10)	26 (7.49)	
Unknown	11 (3.17)	10 (2.88)	9 (2.59)	3 (0.86)	
Cause of death					
Tumor-specific	74 (39.15)	31 (16.40)	38 (20.11)	20 (10.58)	0.460
Non-tumor-specific	11 (5.82)	5 (2.65)	4 (22.22)	6 (3.17)	

Note: \*indicates statistical significance. <sup>#</sup>For statistical purposes, two categories were considered: patients with a prior urothelial tumor history and patients without a prior urothelial tumor history.

F: Female, GU: Genomically unstable, M: Male, NAS: Non-specified, TURBT: Transurethral resection of bladder tumor, URO: Urothelial.

**Table S2. Correlation between immunohistochemically-based subtypes and histopathological variables**

Variables (number of patients=347)	Luminal-like URO-NAS (%)	Luminal-like GU (%)	Basal-like (%)	NULL (%)	p-value
Histological subtypes					
Yes	30 (8.65)	19 (5.48)	45 (12.97)	35 (10.09)	<0.0001*
No	115 (33.14)	62 (17.87)	30 (8.65)	11 (3.17)	
AJCC group staging <sup>~</sup>					
II	24 (6.92)	17 (4.90)	8 (2.31)	5 (1.44)	0.169
IIIA	54 (15.56)	26 (7.49)	40 (11.53)	24 (6.92)	
IIIB/IV	17 (4.90)	8 (2.31)	7 (2.02)	24 (6.92)	
Stromal TILs <sup>~</sup>					
<10%	70 (20.17)	32 (9.22)	18 (5.19)	19 (5.48)	<0.0001*
≥10%	17 (4.90)	15 (4.32)	34 (9.80)	13 (3.75)	
N/A	8 (2.31)	4 (1.15)	3 (0.86)	1 (0.29)	
LVI <sup>~</sup>					
Yes	77 (22.19)	45 (12.97)	46 (13.26)	25 (7.20)	0.706
No	12 (3.46)	4 (1.15)	7 (2.02)	5 (1.44)	
N/A	6 (1.73)	2 (0.58)	2 (0.58)	3 (0.86)	
PNI <sup>~</sup>					
Yes	50 (14.41)	21 (6.05)	27 (7.78)	12 (3.46)	0.267
No	31 (8.93)	20 (5.76)	24 (6.92)	17 (4.90)	
N/A	14 (4.03)	10 (2.88)	4 (1.15)	4 (1.15)	

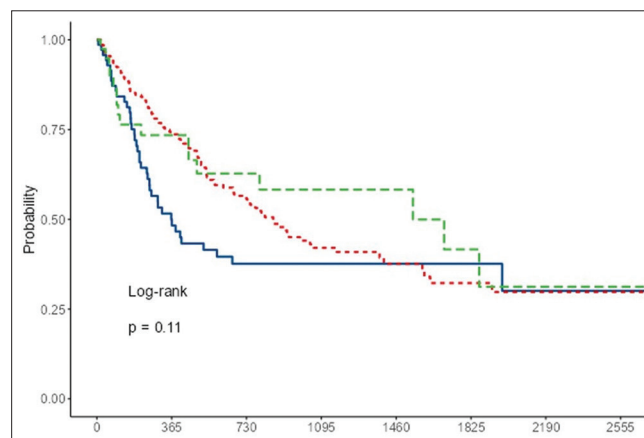
Note: <sup>~</sup>represents the parameter evaluated in radical cystectomy; \*indicates statistical significance.

AJCC: American Joint Commission on Cancer, GU: Genomically unstable, LVI: Linfovascular invasion, NAS: Non-specified, N/A: Not assessable, PNI: Perineural invasion, TILs: Tumor-infiltrating lymphocytes, URO: Urothelial.

**Table S3. Survival analysis: overall and tumor-specific by immunohistochemically-based subtypes (three classes)**

IHC-based subtypes	OS			TSS		
	HR	CI (95%)	P-value	HR	CI (95%)	p-value
Basal-like		-			-	
Luminal-like	0.76	0.54–1.07	0.113	0.71	0.49–1.02	0.062
URO-NAS-GU						
NULL	0.75	0.45–1.24	0.257	0.62	0.35–1.09	0.099

CI: Confidence interval, GU: Genomically unstable, HR: Hazard ratio, IHC: Immunohistochemistry, NAS: Non-specified, OS: Overall survival, TSS: Tumor-specific survival, URO: Urothelial.

**Figure S1.** Kaplan–Meier tumor-specific survival curves by immunohistochemistry-based subtypes (three classes).

Notes: Blue: Basal-like; Green: Luminal-like urothelial-non-specified-genomically unstable; Red: NULL. Time data on the X-axis is expressed in days.

**Table S4. Correlation between IHC-based subtypes and histopathological variables**

Variables (number of patients=347)	Luminal-like URO-NAS (%)	Luminal-like GU (%)	Basal-like (%)	NULL (%)	<i>p</i> -value
Histological subtypes					
Yes	30 (8.65)	19 (5.48)	45 (12.97)	35 (10.09)	<b>&lt;0.0001</b>
No	115 (33.14)	62 (17.87)	30 (8.65)	11 (3.17)	
AJCC group staging <sup>‡</sup>					
II	24 (6.92)	17 (4.90)	8 (2.31)	5 (1.44)	0.169
IIIA	54 (15.56)	26 (7.49)	40 (11.53)	24 (6.92)	
IIIB/IV	17 (4.90)	8 (2.31)	7 (2.02)	4 (1.15)	
Stromal TILs <sup>‡</sup>					
<10%	70 (20.17)	32 (9.22)	18 (5.19)	19 (5.48)	<b>&lt;0.0001</b>
≥10%	17 (4.90)	15 (4.32)	34 (9.80)	13 (3.75)	
N/A	8 (2.31)	4 (1.15)	3 (0.86)	1 (0.29)	
LVI <sup>‡</sup>					
Yes	77 (22.19)	45 (12.97)	46 (13.26)	25 (7.20)	0.706
No	12 (3.46)	4 (1.15)	7 (2.02)	5 (1.44)	
N/A	6 (1.73)	2 (0.58)	2 (0.58)	3 (0.86)	
PNI <sup>‡</sup>					
Yes	50 (14.41)	21 (6.05)	27 (7.78)	12 (3.46)	0.267
No	31 (8.93)	20 (5.76)	24 (6.92)	17 (4.90)	
N/A	14 (4.03)	10 (2.88)	4 (1.15)	4 (1.15)	

Note: <sup>‡</sup>represents the parameter evaluated on radical cystectomy; bold value indicates significance.

IHC: Immunohistochemistry, LVI: Linfovascular invasion, N/A: not assessable, PNI: Perineural invasion.

**Table S5. Survival analysis, overall and tumor-specific: IHC-based subtypes in three classes**

IHC-based subtypes	Overall survival			Tumor-specific survival		
	HR	IC (95%)	<i>P</i> -value	HR	IC (95%)	<i>p</i> -value
Basal-like	-			-		
Luminal-like	0.76	0.54–1.07	0.113	0.71	0.49–1.02	0.062
URO-NAS-GU						
NULL	0.75	0.45–1.24	0.257	0.62	0.35–1.09	0.099

CI: Confidence interval, GU: Genomically unstable, HR: Hazard ratio, IHC: Immunohistochemistry, NAS: Non-specified, URO: Urothelial.