

Supplementary Table 1: Patient-, tumour- and hospital characteristics of patients diagnosed with non-metastatic MIBC between 2005-2019, by treatment

	Total		Treatment		p-value*		
			Untreated			Treated	
	N	(%)	N	(%)		N	(%)
Total	15047	(100.0)	3236	(21.5)	11811	(78.5)	
Patient characteristics							
Gender							0.0002
Male	10990	(73.0)	2282	(70.5)	8708	(73.7)	
Female	4057	(27.0)	954	(29.5)	3103	(26.3)	
Age at diagnosis (median, IQR)	74.0	66.0-81.0	82.0	75.0-86.0	72.0	66.0-81.0	<.0001
Age at diagnosis							<.0001
<75 years	7819	(52.0)	777	(24.0)	7042	(59.6)	
≥75 years	7228	(48.0)	2459	(76.0)	4769	(40.4)	
Weighted Charlson Comorbidity Index							<.0001
0	1455	(36.5)	184	(23.7)	1271	(39.7)	
1	1101	(27.6)	213	(27.4)	888	(27.7)	
2	607	(15.2)	153	(19.7)	454	(14.2)	
3 or more	499	(12.5)	166	(21.3)	333	(10.4)	
Unknown	320	(8.0)	62	(8.0)	258	(8.1)	
Type of comorbidity							
Diabetes	641	(29.0)	160	(30.1)	481	(28.7)	0.5476
Chronic pulmonary disease	613	(27.8)	160	(30.1)	453	(27.0)	0.1740
Myocardial infarct	447	(20.3)	91	(17.1)	356	(21.3)	0.0381
Peripheral vascular disease	473	(21.4)	122	(22.9)	351	(21.0)	0.3330
Any tumour	357	(16.2)	97	(18.2)	260	(15.5)	0.1391
Cerebrovascular disease	414	(18.8)	125	(23.5)	289	(17.3)	0.0013
Moderate or severe renal disease	274	(12.4)	79	(14.8)	195	(11.6)	0.0506
Congestive heart failure	152	(6.9)	64	(12.0)	88	(5.3)	<.0001
Ulcer disease	99	(4.5)	30	(5.6)	69	(4.1)	0.1401
Connective tissue disease	92	(4.2)	17	(3.2)	75	(4.5)	0.1974
Dementia	77	(3.5)	48	(9.0)	29	(1.7)	<.0001
Metastatic solid tumour (other than bladder cancer)	38	(1.7)	21	(3.9)	17	(1.0)	<.0001
Mild liver disease	34	(1.5)	6	(1.1)	28	(1.7)	0.3749
Diabetes with end organ damage	43	(1.9)	12	(2.3)	31	(1.9)	0.5561
Hemiplegia or paraplegia	19	(0.9)	8	(1.5)	11	(0.7)	0.0654
HIV	5	(0.2)	-	-	5	(0.3)	0.2071
Socio-economic status (SES)							<.0001
Low	4956	(32.9)	1291	(39.9)	3665	(31.0)	
Middle	4707	(31.3)	888	(27.4)	3819	(32.3)	
High	3603	(23.9)	588	(18.2)	3015	(25.5)	
Unknown	1781	(11.8)	469	(14.5)	1312	(11.1)	
Tumour characteristics							
cT stage (TNM)							<.0001
cT2	11664	(77.5)	2525	(78.0)	9139	(77.4)	
cT3	2362	(15.7)	402	(12.4)	1960	(16.6)	
cT4a	1021	(6.8)	309	(9.5)	712	(6.0)	
Focality of the tumour							<.0001
Multifocal	3009	(20.0)	667	(20.6)	2342	(19.8)	
Unifocal	11059	(73.5)	2240	(69.2)	8819	(74.7)	

Unknown	979 (6.5)	329 (10.2)	650 (5.5)	
Localisation of the tumour				<.0001
Trigone	1091 (7.3)	256 (7.9)	835 (7.1)	
Dome	622 (4.1)	113 (3.5)	509 (4.3)	
Right or left wall	3490 (23.2)	693 (21.4)	2797 (23.7)	
Anterior wall	399 (2.7)	85 (2.6)	314 (2.7)	
Posterior wall	979 (6.5)	191 (5.9)	788 (6.7)	
Bladder neck	572 (3.8)	134 (4.1)	438 (3.7)	
Left or right ureteral orifice	844 (5.6)	167 (5.2)	677 (5.7)	
Overlapping localisations	5449 (36.2)	1161 (35.9)	4288 (36.3)	
Unknown	1601 (10.6)	436 (13.5)	1165 (9.9)	
Hospital characteristics				
Type of hospital (diagnosis)				0.0027
Community hospital	6385 (42.4)	1408 (43.5)	4977 (42.1)	
Non-university referral hospital	7831 (52.0)	1688 (52.2)	6143 (52.0)	
University hospital	831 (5.5)	140 (4.3)	691 (5.9)	

IQR: Interquartile range

* P-value was calculated using Chi-square for categorical variables and ANOVA for continuous variables

Supplementary Table 2: Patient- and tumour characteristics of untreated and treated patients in the BlaZIB cohort after propensity score matching*

	Total		Treatment		p-value**		
			Untreated	Treated			
	N	(%)	N	(%)	N	(%)	
Total	674	(100.0)	337	(50.0)	337	(50.0)	
Patient characteristics							
Gender						0.4559	
Male	461	(68.4)	235	(69.7)	226	(67.1)	
Female	213	(31.6)	102	(30.3)	111	(32.9)	
Age at diagnosis (median, IQR)	81.0	76.0-85.0	82.0	76.0-86.0	80.0	76.0-85.0	0.3135
Body Mass Index (median, IQR)	24.8	22.4-28.1	24.8	22.3-27.7	25.0	22.7-28.4	0.8989
Weighted Charlson Comorbidity Index						0.8333	
0	165	(24.5)	79	(23.4)	86	(25.5)	
1	195	(28.9)	101	(30.0)	94	(27.9)	
2	149	(22.1)	77	(22.8)	72	(21.4)	
3 or more	165	(24.5)	80	(23.7)	85	(25.2)	
Performance status						0.8969	
ECOG 0	120	(17.8)	62	(18.4)	58	(17.2)	
ECOG 1	190	(28.2)	93	(27.6)	97	(28.8)	
ECOG 2 or higher	364	(54.0)	182	(54.0)	182	(54.0)	
Renal function (eGFR, mL/min/1.73m²)	54.0	37.0-69.0	54.0	35.0-72.0	54.0	39.2-68.0	0.5793
Socio-economic status (SES)						0.0314	
Low	284	(42.1)	127	(37.7)	157	(46.6)	
Middle	241	(35.8)	124	(36.8)	117	(34.7)	
High	149	(22.1)	86	(25.5)	63	(18.7)	
Previous surgery						0.7277	
Yes	180	(26.7)	88	(26.1)	92	(27.3)	
No	494	(73.3)	249	(73.9)	245	(72.7)	
Previous radiation						0.8798	
Yes	47	(7.0)	23	(6.8)	24	(7.1)	
No	627	(93.0)	314	(93.2)	313	(92.9)	
Tumour characteristics							
cT stage (TNM)						0.6904	
cT2	475	(70.5)	241	(71.5)	234	(69.4)	
cT3	143	(21.2)	67	(19.9)	76	(22.6)	
cT4a	56	(8.3)	29	(8.6)	27	(8.0)	
Focality of the tumour						0.4388	
Multifocal	187	(27.7)	98	(29.1)	89	(26.4)	
Unifocal	487	(72.3)	239	(70.9)	248	(73.6)	

IQR: Interquartile range; ECOG: Eastern Cooperative Oncology Group; eGFR: estimated glomerular filtration rate; MDTM: Multidisciplinary team meeting

* Patients were matched on age, body mass index, renal function, performance status, tumour stage, and previous radiation in abdomen/pelvic area

** P-value was calculated using Chi-square for categorical variables and ANOVA for continuous variables

Supplementary Table 3: Uni- and multivariable Cox Proportional Hazards regression analyses on the association between patient-, tumour- and hospital characteristics and survival, in patients diagnosed with non-metastatic MIBC between 1 November 2017 and 31 October 2019, included in the BlaZIB study

	Univariable model					
	overall HR 95% CI		<75 years HR 95% CI		≥75 years HR 95% CI	
Treatment	ref.	ref.	ref.	ref.	ref.	ref.
Treated	4.71	4.08 - 5.43	6.61	4.89 - 8.93	3.24	2.73 - 3.84
Untreated						
Propensity score (continuous)	14.62	10.73 - 19.93	639.34	140.93 - 2900.36	7.95	5.26 - 12.01
	Multivariable model 1*					
	overall HR 95% CI		<75 years HR 95% CI		≥75 years HR 95% CI	
Treatment	ref.	ref.	ref.	ref.	ref.	ref.
Treated	2.78	2.31 - 3.36	4.06	2.80 - 5.87	2.40	1.96 - 2.95
Untreated						
Propensity score (continuous)	5.36	3.67 - 7.83	178.69	36.00 - 887.02	3.43	2.12 - 5.55
	Multivariable model 2**					
	overall HR 95% CI		<75 years HR 95% CI		≥75 years HR 95% CI	
Treatment	ref.	ref.	ref.	ref.	ref.	ref.
Treated	2.88	2.38 - 3.47	4.79	3.33 - 6.90	2.46	1.98 - 3.05
Untreated						
Propensity score (continuous)	0.22	0.07 - 0.65	8.92	0.16 - 508.91	0.70	0.02 - 30.31

HR: Hazard Ratio; 95% CI: 95% Confidence Interval; ECOG: Eastern Cooperative Oncology Group; eGFR: estimated glomerular filtration rate; MDTM: Multidisciplinary team meeting

* Multivariable model 1 includes treatment (yes/no) and propensity score

** Multivariable model 2 includes treatment (yes/no), propensity score, gender, age, body mass index, Weighted Charlson Comorbidity Index, performance status, renal function, socio-economic status, tumour stage, whether the patient was discussed in a MDTM, previous surgery in abdomen/pelvic area, previous radiation in abdomen/pelvic area