

Study	N patients	Patient Characteristics	Follow-up	Outcomes	Prognostic factors	Comments	
Sylvester 2006	2596 (from 7 EORTC randomised trials comparing prophylactic treatments after TUR) Median age =65 years 79% M / 20% F / 1% unknown	Intravesical treatment	Median 3.9 years, maximum 14.8 years	Time to first recurrence Time to progression	Age Gender Prior treatment Prior recurrence rate No. of tumours Tumour size T category Presence of CIS Grade T1G3 Recurrence at 3 months		
		No					561 (21.6)
		Yes					2035 (78.4)
		Prior treatment					
		No					2358 (90.8)
		Yes					187 (7.2)
		Prior recurrence rate					
		Primary					1405 (54.1)
		Recurrent ≤1 rec/yr					505 (19.5)
		Recurrent >1 rec/yr					645 (24.8)
		N tumours					
		1					1405 (54.1)
		2-7					836 (32.2)
		≥8					255 (9.8)
		Tumour size					
		<1cm					920 (53.4)
		<3cm					1167 (45)
		≥3cm					464 (17.9)
		T category					
		Ta					1451 (55.9)
		T1					1108 (42.7)
		Carcinoma in situ					
		No					2440 (94)
Yes	113 (4.4)						
Grade							
G1	1121 (43.2)						
G2	1139 (43.9)						

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Fernandez-Gomez 2008	<p>N=1062 (from 4 randomised trials of intravesical therapy)</p> <p>Median age 66 yrs</p> <p>90% M / 10% F</p> <p>All received BCG, Connaught strain, weekly for 6 wks, then every 2 wks x6.</p> <p>33% had recurrence, 13% progressed into MIBC</p>	<table border="1"> <tr><td colspan="2">T category n(%)</td></tr> <tr><td>Ta</td><td>214 (20.2)</td></tr> <tr><td>T1</td><td>848 (79.8)</td></tr> <tr><td colspan="2">Recurrent tumour</td></tr> <tr><td>No</td><td>706 (66.5)</td></tr> <tr><td>Yes</td><td>356 (33.5)</td></tr> <tr><td colspan="2">Grade</td></tr> <tr><td>G1</td><td>167 (15.7)</td></tr> <tr><td>G2</td><td>629 (59.2)</td></tr> <tr><td>G3</td><td>266 (25)</td></tr> <tr><td colspan="2">No. of tumours</td></tr> <tr><td>1</td><td>535 (50.4)</td></tr> <tr><td>2-3</td><td>278 (26.2)</td></tr> <tr><td>4-7</td><td>160 (15.1)</td></tr> <tr><td>≥8</td><td>89 (8.4)</td></tr> </table>	T category n(%)		Ta	214 (20.2)	T1	848 (79.8)	Recurrent tumour		No	706 (66.5)	Yes	356 (33.5)	Grade		G1	167 (15.7)	G2	629 (59.2)	G3	266 (25)	No. of tumours		1	535 (50.4)	2-3	278 (26.2)	4-7	160 (15.1)	≥8	89 (8.4)	Median 69 mo	Recurrence Progression (to stage T2 or higher)	Age Primary vs. recurrent tumour No. and size of tumour Doses of BCG and no. of instillations T category Grade Presence of CIS Recurrence at 1 st cystoscopy					
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Miyake 2011 Japan	N=130 88% M/12% F Newly diagnosed NMIBC 1998-2009. 75/130 (58%) received adjuvant therapy after TURBT: 67 BCG, 8 epirubicin.	<table border="1"> <tr><td colspan="2">T category n(%)</td></tr> <tr><td>Ta</td><td>104 (80)</td></tr> <tr><td>T1</td><td>26 (20)</td></tr> <tr><td colspan="2">Grade WHO 2004</td></tr> <tr><td>PUNLMP</td><td>13 (10)</td></tr> <tr><td>LG</td><td>84 (65)</td></tr> <tr><td>HG</td><td>33 (25)</td></tr> <tr><td colspan="2">Concomitant CIS</td></tr> <tr><td>No</td><td>123 (95)</td></tr> <tr><td>Yes</td><td>7 (5)</td></tr> <tr><td colspan="2">Lymphovascular involvement</td></tr> <tr><td>No</td><td>110 (85)</td></tr> <tr><td>Yes</td><td>20 (15)</td></tr> <tr><td colspan="2">Multiplicity</td></tr> <tr><td>Solitary</td><td>70 (54)</td></tr> <tr><td>multiple</td><td>60 (46)</td></tr> <tr><td colspan="2">Tumour diameter</td></tr> <tr><td><3</td><td>99 (76)</td></tr> <tr><td>≥3</td><td>31 (24)</td></tr> </table>	T category n(%)		Ta	104 (80)	T1	26 (20)	Grade WHO 2004		PUNLMP	13 (10)	LG	84 (65)	HG	33 (25)	Concomitant CIS		No	123 (95)	Yes	7 (5)	Lymphovascular involvement		No	110 (85)	Yes	20 (15)	Multiplicity		Solitary	70 (54)	multiple	60 (46)	Tumour diameter		<3	99 (76)	≥3	31 (24)	Median 36 mo (range 1-140 mo)	Progression (to muscle invasive disease, or a metastatic site in other organs) Recurrence (after resection)	T stage Tumour grade CIS Lymphovascular involvement Endophytic growth pattern Von Brunn's nest involvement Multiplicity Tumour diameter (cm) Intravesical therapy	
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Kwon 2012 Korea	N=406 Mean age 64.4±11.4	<table border="1"> <tr><td colspan="2">T category n(%)</td></tr> <tr><td>Ta</td><td>274 (67.5)</td></tr> </table>	T category n(%)		Ta	274 (67.5)	Median 76.9 mo (range 12-167 mo)	Recurrence Progression (shift to stage ≥T2)	Age Gender Underlying diseases																																			
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	<p>years</p> <p>84% M / 17% F</p> <p>Patients with NMIBC who underwent TURBT 1999-2010. Must have tumour resection weight available. Excluded: CIS, no BCG, evidence of metastases</p> <p>One immediate intravesical chemo done among the included patients</p>	<table border="1"> <tr><td>T1</td><td>132 (32.5)</td></tr> <tr><td>Grade WHO 2004</td><td></td></tr> <tr><td>Low</td><td>165 (41)</td></tr> <tr><td>High</td><td>241 (59.4)</td></tr> <tr><td>Tumour weight</td><td></td></tr> <tr><td>≥2</td><td>241 (59)</td></tr> <tr><td><2</td><td>165 (41)</td></tr> <tr><td>Lymphovascular involvement</td><td></td></tr> <tr><td>No</td><td>394 (97)</td></tr> <tr><td>Yes</td><td>12 (3)</td></tr> <tr><td>No. of tumours</td><td></td></tr> <tr><td>1-3</td><td>103 (25)</td></tr> <tr><td>>3</td><td>303 (75)</td></tr> <tr><td>Tumour size (cm)</td><td></td></tr> <tr><td>≥3</td><td>192 (47)</td></tr> <tr><td><3</td><td>214 (53)</td></tr> </table>	T1	132 (32.5)	Grade WHO 2004		Low	165 (41)	High	241 (59.4)	Tumour weight		≥2	241 (59)	<2	165 (41)	Lymphovascular involvement		No	394 (97)	Yes	12 (3)	No. of tumours		1-3	103 (25)	>3	303 (75)	Tumour size (cm)		≥3	192 (47)	<3	214 (53)			<p>Cancer stage</p> <p>Grade</p> <p>Multiplicity</p> <p>Size</p> <p>Lymphovascular invasion</p> <p>Resection weight</p>									
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<p>Cho 2009</p> <p>Korea</p>	<p>N=118</p> <p>Median age 67 (range 39-91) years</p> <p>86% M / 14% F</p> <p>Newly diagnosed T1 bladder UC. Repeat TURBT 31 (26%), 100 (85%) intravesical therapy: 65 MMC, 27 BCG (6-wk), 8 epirubicin. Systemic chemo recommended in patients with multifocal LVI. 11 patients had 2-3 cycles of cisplatin based chemo. 4 patient had RC</p>	<table border="1"> <tr><td>Tumour Grade n(%)</td><td></td></tr> <tr><td>1</td><td>3 (2.5)</td></tr> <tr><td>2</td><td>60 (50.8)</td></tr> <tr><td>3</td><td>55 (46.6)</td></tr> <tr><td>CIS</td><td></td></tr> <tr><td>No</td><td>113 (95.8)</td></tr> <tr><td>Yes</td><td>5 (4.2)</td></tr> <tr><td>Lymphovascular involvement</td><td></td></tr> <tr><td>No</td><td>85 (72)</td></tr> <tr><td>Yes</td><td>33 (28)</td></tr> <tr><td>No. of tumours</td><td></td></tr> <tr><td><4</td><td>57 (48)</td></tr> <tr><td>≥4</td><td>61 (52)</td></tr> <tr><td>Tumour size (cm)</td><td></td></tr> <tr><td><3</td><td>70 (59)</td></tr> <tr><td>≥3</td><td>48 (41)</td></tr> <tr><td>Repeat TURBT</td><td></td></tr> <tr><td>No</td><td>87 (74)</td></tr> <tr><td>Yes</td><td>31 (26)</td></tr> <tr><td>Intravesical therapy</td><td></td></tr> </table>	Tumour Grade n(%)		1	3 (2.5)	2	60 (50.8)	3	55 (46.6)	CIS		No	113 (95.8)	Yes	5 (4.2)	Lymphovascular involvement		No	85 (72)	Yes	33 (28)	No. of tumours		<4	57 (48)	≥4	61 (52)	Tumour size (cm)		<3	70 (59)	≥3	48 (41)	Repeat TURBT		No	87 (74)	Yes	31 (26)	Intravesical therapy		Median 35 mo (range 12-89)	<p>Recurrence</p> <p>Progression (muscularis propria invasion by UC and/or new onset metastatic disease.</p>	<p>Lymphovascular invasion (considered present only when tumour cells were unequivocally noted within or attached to the wall of a vascular or lymphatic space on hematoxylin and eosin stained sections)</p> <p>Gender</p> <p>Age</p> <p>Bladder tumour history</p> <p>Tumour size</p> <p>No. Tumours</p> <p>Tumour grade</p> <p>CIS</p> <p>Repeat TUR</p> <p>Intravesical therapy</p> <p>Systemic therapy</p>	
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		No	Yes				
		No	18 (15)				
		Yes	100 (85)				
		Recurrence					
		No	73 (62)				
		Yes	45 (38)				
		Progression					
		No	99 (84)				
		Yes	19 (16)				
Brimo 2013 Canada	N=86 Mean age 71 years Patients with pT1 and treated with TURBT 2004-2012	All urothelial carcinoma except 3 micropapillary and 1 sarcomatoid. 13% lymphovascular invasion. None had history of invasive UC. Repeat TUR not routinely performed if there was adequate muscularis propria in the specimen and was left to discretion of urologist.		Mean 29 months	Recurrence (any subsequent lesion including CIS and noninvasive papillary neoplasms) Progression (pT2 in subsequent TURB specimens)	Muscularis mucosa invasion Millimetric depth of invasion Total diameter of invasive carcinoma No of fragments containing invasion Lymphovascular invasion (considered present only if it was unequivocally present on hematoxylin and eosin sections) Concomitant CIS Histological subtype	Unclear whether patients received adjuvant intravesical therapy
Scosyrev 2009 USA	N=1422 patients with pure squamous cell carcinoma N=107613 urothelial carcinomas for comparison	85% of SCCs were muscle invasive. 22% of UCs were muscle invasive. SCC Stage 1 n=104, UC Stage 1 n=21462. Mean age SCC =74 yrs, UC=72 yrs Women (%) SCC=54, UC=23 High grade (%) SCC=39, UC=59 Cystectomy (%) SCC =17.3, UC=6.1 Radiotherapy (%) SCC=10.6, UC =1.9		2 years	All-cause mortality Bladder cancer specific mortality	Histologic type (UC vs. pure SCC) Age Gender Race AJCC stage Grade (well/moderately/poorly differentiated, undifferentiated) Treatment (cystectomy, radiotherapy)	Modified least squares model with identity link function and robust variance estimator used rather than Cox model
Lopez 1995 Spain	N=170 T1 bladder tumours undergoing TUR	17/170 (10%) displayed unequivocal vascular invasion. 15 Male, 2 female. Aged between 60-71 (mean age 69.5)		Mean 47 mo, range 18-86 mo	Overall survival	Lymphovascular invasion (H&E staining, present when tumour cells were unequivocally noted within or	

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	followed by long term instillations of either MMC or adriamycin.	Vascular invasion was confined to the lamina propria in 16 cases, and extended into the level of muscularis propria in one case.			attached to the wall of a vascular or lymphatic space. All positive cases verified using immunohistochemistry) Grade Presence of papillary phenotype Tumour size																																																			
Palou 2012	N=146 Mean age 64.9 years (range 25-81) 88% M / 12% F All T1G3 (1985-1996) underwent complete TUR with muscle in specimen. No second TURBT. One induction course of BCG (81mg, Connaught) without maintenance treatment. 65 (44.5%) have recurrence 25 (17.1%) have progressed 56 (38.4%) died 18 (12.3%) died from BCa	<table border="1"> <tr><td colspan="2">Substage n(%)</td></tr> <tr><td>T1a</td><td>48 (32.9)</td></tr> <tr><td>T1b</td><td>23 (15.7)</td></tr> <tr><td>T1c</td><td>22 (15.1)</td></tr> <tr><td>T1x</td><td>53 (36.3)</td></tr> <tr><td colspan="2">Tumour diameter (cm)</td></tr> <tr><td><1.5</td><td>42 (28.8)</td></tr> <tr><td>1.5-3</td><td>63 (43.1)</td></tr> <tr><td>>3</td><td>41 (28.1)</td></tr> <tr><td colspan="2">Concomitant CIS</td></tr> <tr><td>Yes</td><td>95 (65.1)</td></tr> <tr><td>No</td><td>51 (34.9)</td></tr> <tr><td colspan="2">CIS in prostatic urethra</td></tr> <tr><td>Yes</td><td>15 (10.3)</td></tr> <tr><td>No</td><td>131 (89.7)</td></tr> <tr><td colspan="2">Multifocal disease</td></tr> <tr><td>Yes</td><td>74 (50.7)</td></tr> <tr><td>No</td><td>72 (49.3)</td></tr> <tr><td colspan="2">Tumour aspect</td></tr> <tr><td>Papillary</td><td>105 (71.9)</td></tr> <tr><td>Solid</td><td>41 (28.1)</td></tr> <tr><td colspan="2">Female or prostatic urethra</td></tr> <tr><td>Yes</td><td>33 (22.6)</td></tr> <tr><td>No</td><td>111 (76)</td></tr> <tr><td>Unknown</td><td>2 (1.4)</td></tr> </table>	Substage n(%)		T1a	48 (32.9)	T1b	23 (15.7)	T1c	22 (15.1)	T1x	53 (36.3)	Tumour diameter (cm)		<1.5	42 (28.8)	1.5-3	63 (43.1)	>3	41 (28.1)	Concomitant CIS		Yes	95 (65.1)	No	51 (34.9)	CIS in prostatic urethra		Yes	15 (10.3)	No	131 (89.7)	Multifocal disease		Yes	74 (50.7)	No	72 (49.3)	Tumour aspect		Papillary	105 (71.9)	Solid	41 (28.1)	Female or prostatic urethra		Yes	33 (22.6)	No	111 (76)	Unknown	2 (1.4)	Median 8.7 years, maximum 13.9 years	Recurrence Progression (≥T2 or metastatic disease) Cancer-specific survival	Age Gender Multiplicity (single or multiple) Largest diameter (<1.5cm, 1.5-3cm, >3cm) Tumour aspect (Papillary or solid) Substage (T1a,T1b, T1c) Concomitant CIS CIS in prostatic urethra	
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Van Rhijn 2010	N=230 Mean age 65.1±12.3 yr 76% M/ 24% F	<table border="1"> <tr><td colspan="2">Stage n(%)</td></tr> <tr><td>Ta</td><td>171(74)</td></tr> <tr><td>T1</td><td>59 (26)</td></tr> <tr><td colspan="2">Tumour diameter</td></tr> </table>	Stage n(%)		Ta	171(74)	T1	59 (26)	Tumour diameter		Median 8.62 years, IQR 6.6-11.8 yrs.	Recurrence Progression Disease-specific survival	Gender Age Hospital Stage Grade	Validation of EORTC risk groups																																										
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Study	N patients	Patient Characteristics	Follow-up	Outcomes	Prognostic factors	Comments																																																																				
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Van Rhijn 2012 1984-2006	N=129 Mean (SD) age 68.8 (9.9)	<table border="1"> <tr><td colspan="2">Sub-stage n(%)</td></tr> <tr><td>T1a</td><td>79 (61)</td></tr> <tr><td>T1b</td><td>17 (13)</td></tr> </table>	Sub-stage n(%)		T1a	79 (61)	T1b	17 (13)	Median 6.5 years	Recurrence Progression (≥pT2 and/or metastases)	Size Multiplicity Hospital Gender																																																															
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Study	N patients	Patient Characteristics	Follow-up	Outcomes	Prognostic factors	Comments																																																												
Netherlands	81% M / 19% F All T1. All patients had induction BCG. No single instillation or random biopsies	<table border="1"> <tr><td>T1c</td><td>33 (26)</td></tr> <tr><td>Tumour size</td><td></td></tr> <tr><td>≤3cm</td><td>67 (52)</td></tr> <tr><td>>3</td><td>62 (48)</td></tr> <tr><td>Concomitant CIS</td><td></td></tr> <tr><td>No</td><td>84 (65)</td></tr> <tr><td>Yes</td><td>45 (35)</td></tr> <tr><td>Multiplicity</td><td></td></tr> <tr><td>Solitary</td><td>77 (60)</td></tr> <tr><td>Multiple (2-7)</td><td>52 (40)</td></tr> <tr><td>Grade (WHO 1973)</td><td></td></tr> <tr><td>G2</td><td>55 (43)</td></tr> <tr><td>G3</td><td>74 (57)</td></tr> <tr><td>Grade (WHO 2004)</td><td></td></tr> <tr><td>LG</td><td>26 (20)</td></tr> <tr><td>HG</td><td>103 (80)</td></tr> <tr><td>EORTC recurrence</td><td></td></tr> <tr><td>Intermediate</td><td>122 (95)</td></tr> <tr><td>High risk</td><td>7 (5)</td></tr> <tr><td>EORTC progression</td><td></td></tr> <tr><td>Intermediate</td><td>16 (12)</td></tr> <tr><td>High</td><td>113 (88)</td></tr> <tr><td>Instillation type</td><td></td></tr> <tr><td>BCG</td><td>106 (82)</td></tr> <tr><td>BCG + chemo</td><td>23 (18)</td></tr> <tr><td>No. of instillations</td><td></td></tr> <tr><td>4-6</td><td>32 (25)</td></tr> <tr><td>7-12</td><td>32 (25)</td></tr> <tr><td>13-18</td><td>26 (20)</td></tr> <tr><td>>18</td><td>39 (30)</td></tr> </table>	T1c	33 (26)	Tumour size		≤3cm	67 (52)	>3	62 (48)	Concomitant CIS		No	84 (65)	Yes	45 (35)	Multiplicity		Solitary	77 (60)	Multiple (2-7)	52 (40)	Grade (WHO 1973)		G2	55 (43)	G3	74 (57)	Grade (WHO 2004)		LG	26 (20)	HG	103 (80)	EORTC recurrence		Intermediate	122 (95)	High risk	7 (5)	EORTC progression		Intermediate	16 (12)	High	113 (88)	Instillation type		BCG	106 (82)	BCG + chemo	23 (18)	No. of instillations		4-6	32 (25)	7-12	32 (25)	13-18	26 (20)	>18	39 (30)			Age CIS Grade (WHO 2004/1973) EORTC recurrence and progression T1 Sub-stage Molecular markers (FGFR3, Ki-67, P27)	
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Seo 2010 Korea 1993-2007	N=251 57% ≤65 years 43% >65 years 76% M / 24% F All received BCG	<table border="1"> <tr><td>Stage n(%)</td><td></td></tr> <tr><td>Ta</td><td>44 (20.1)</td></tr> <tr><td>T1</td><td>175 (79.9)</td></tr> <tr><td>Tumour diameter</td><td></td></tr> <tr><td><3cm</td><td>155 (61.8)</td></tr> <tr><td>≥3</td><td>96 (38.2)</td></tr> <tr><td>CIS</td><td></td></tr> </table>	Stage n(%)		Ta	44 (20.1)	T1	175 (79.9)	Tumour diameter		<3cm	155 (61.8)	≥3	96 (38.2)	CIS		Mean 68.9 months, range 12-204 months	Recurrence Progression	NA Recurrence and progression rates were compared with the values presented in the EORTC tables.																																															
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Sakano 2010 Japan 2004-2006	<p>N=592 (372 classified into EORTC risk groups)</p> <p>Median age 73 (33-95)</p> <p>79% M / 20% F</p> <p>Primary CIS and patients with systemic chemo or radiotherapy or cystectomy after TUR excluded</p> <p>189 (32%) received intravesical chemo, 92 (15.5%) BCG. No maintenance BCG</p>	<table border="1"> <tr><td colspan="2">Stage n(%)</td></tr> <tr><td>Ta</td><td>287 (48.5)</td></tr> <tr><td>T1</td><td>305 (51.5)</td></tr> <tr><td colspan="2">Tumour size</td></tr> <tr><td>≤3cm</td><td>562 (94.9)</td></tr> <tr><td>> 3cm</td><td>25 (4.2)</td></tr> <tr><td colspan="2">Concomitant CIS</td></tr> <tr><td>No</td><td>360 (60.8)</td></tr> <tr><td>Yes</td><td>53 (9.0)</td></tr> <tr><td>Unknown</td><td>179 (30.2)</td></tr> <tr><td colspan="2">No. of tumours</td></tr> <tr><td>1</td><td>304 (51.5)</td></tr> <tr><td>2-7</td><td>264 (44.6)</td></tr> <tr><td>≥8</td><td>22 (3.7)</td></tr> <tr><td colspan="2">Grade (WHO 1973)</td></tr> <tr><td>G1</td><td>105 (17.7)</td></tr> <tr><td>G2</td><td>334 (56.4)</td></tr> <tr><td>G3</td><td>145 (24.5)</td></tr> <tr><td colspan="2">Prior recurrence rate</td></tr> <tr><td>Primary</td><td>353 (59.6)</td></tr> <tr><td>≤1 rec/year</td><td>108 (18.2)</td></tr> <tr><td>>1 rec/year</td><td>85 (14.4)</td></tr> <tr><td>unknown</td><td>46 (7.8)</td></tr> </table>	Stage n(%)		Ta	287 (48.5)	T1	305 (51.5)	Tumour size		≤3cm	562 (94.9)	> 3cm	25 (4.2)	Concomitant CIS		No	360 (60.8)	Yes	53 (9.0)	Unknown	179 (30.2)	No. of tumours		1	304 (51.5)	2-7	264 (44.6)	≥8	22 (3.7)	Grade (WHO 1973)		G1	105 (17.7)	G2	334 (56.4)	G3	145 (24.5)	Prior recurrence rate		Primary	353 (59.6)	≤1 rec/year	108 (18.2)	>1 rec/year	85 (14.4)	unknown	46 (7.8)	Median 37 months, range 3-69	Recurrence	<p>Age</p> <p>ECOG PS</p> <p>Prior recurrence rate</p> <p>No. of tumours</p> <p>T category</p> <p>Grade</p> <p>Gender</p> <p>Tumour size</p> <p>Concomitant CIS</p> <p>Histopathology</p> <p>Intravesical therapy</p> <p>Recurrence-free survival curves were also plotted for the EORTC risk groups</p>	
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Hernandez 2011 Spain 1998-2008	N=417 Mean age 68.8 years 84% M / 16% F	<table border="1"> <tr><td colspan="2">Stage n(%)</td></tr> <tr><td>Ta</td><td>227 (58.1)</td></tr> <tr><td>T1</td><td>164 (41.9)</td></tr> <tr><td colspan="2">Tumour size</td></tr> <tr><td><3cm</td><td>223 (59.8)</td></tr> <tr><td>≥3cm</td><td>150 (40.2)</td></tr> <tr><td colspan="2">Concomitant CIS</td></tr> <tr><td>Yes</td><td>14 (3.4)</td></tr> <tr><td>No</td><td>403 (96.6)</td></tr> <tr><td colspan="2">No. of tumours</td></tr> <tr><td>1</td><td>283 (70.8)</td></tr> <tr><td>2-7</td><td>115 (28.8)</td></tr> <tr><td>>7</td><td>2 (0.5)</td></tr> <tr><td colspan="2">Grade (WHO 1973)</td></tr> <tr><td>G1</td><td>220 (54.7)</td></tr> <tr><td>G2</td><td>142 (35.3)</td></tr> <tr><td>G3</td><td>40 (10)</td></tr> <tr><td colspan="2">Prior recurrence rate</td></tr> <tr><td>Primary</td><td>219 (52.5)</td></tr> <tr><td><1 rec/year</td><td>167 (40)</td></tr> <tr><td>>1 rec/year</td><td>31 (7.4)</td></tr> <tr><td colspan="2">Intravesical therapy</td></tr> <tr><td>MMC single</td><td>274 (70.3)</td></tr> </table>	Stage n(%)		Ta	227 (58.1)	T1	164 (41.9)	Tumour size		<3cm	223 (59.8)	≥3cm	150 (40.2)	Concomitant CIS		Yes	14 (3.4)	No	403 (96.6)	No. of tumours		1	283 (70.8)	2-7	115 (28.8)	>7	2 (0.5)	Grade (WHO 1973)		G1	220 (54.7)	G2	142 (35.3)	G3	40 (10)	Prior recurrence rate		Primary	219 (52.5)	<1 rec/year	167 (40)	>1 rec/year	31 (7.4)	Intravesical therapy		MMC single	274 (70.3)	Median 59 months	Recurrence Progression (to muscle-invasive status)	Same as Sylvester (2006) EORTC study	Validation of EORTC tables
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14-23	15 (3.7)																																																			
Altieri 2012 Italy 2002-2011	<p>N=259</p> <p>Median age 71 (43-90)</p> <p>78% M / 22% F</p> <p>73% of all patients had single MMC 40mg. 57% intermediate risk induction and 12-month maintenance chemo and 23% BCG. 87.5% high risk induction and 12-mo maintenance BCG. 22% re-TURB. All high risk patients received re-TUR.</p>	<table border="1"> <tr><td colspan="2">Stage n(%)</td></tr> <tr><td>Ta</td><td>161(62.2)</td></tr> <tr><td>T1</td><td>98 (37.8)</td></tr> <tr><td colspan="2">Tumour size</td></tr> <tr><td><3cm</td><td>227 (87.6)</td></tr> <tr><td>≥3cm</td><td>32 (12.4)</td></tr> <tr><td colspan="2">Concomitant CIS</td></tr> <tr><td>Yes</td><td>7 (2.7)</td></tr> <tr><td colspan="2">No. of tumours</td></tr> <tr><td>1</td><td>131 (50.6)</td></tr> <tr><td>2-7</td><td>115 (44.4)</td></tr> <tr><td>≥8</td><td>13 (5)</td></tr> <tr><td colspan="2">Grade (WHO 1973)</td></tr> <tr><td>G1</td><td>94 (36.3)</td></tr> <tr><td>G2</td><td>114 (44)</td></tr> <tr><td>G3</td><td>51 (19.7)</td></tr> <tr><td colspan="2">Recurrence</td></tr> <tr><td>Primary</td><td>185 (71.4)</td></tr> <tr><td>Recurrent</td><td>74 (28.6)</td></tr> <tr><td colspan="2">Intravesical therapy</td></tr> <tr><td>MMC single dose</td><td>189 (73)</td></tr> <tr><td colspan="2">EORTC recurrence score</td></tr> <tr><td>0</td><td>38 (14.7)</td></tr> </table>	Stage n(%)		Ta	161(62.2)	T1	98 (37.8)	Tumour size		<3cm	227 (87.6)	≥3cm	32 (12.4)	Concomitant CIS		Yes	7 (2.7)	No. of tumours		1	131 (50.6)	2-7	115 (44.4)	≥8	13 (5)	Grade (WHO 1973)		G1	94 (36.3)	G2	114 (44)	G3	51 (19.7)	Recurrence		Primary	185 (71.4)	Recurrent	74 (28.6)	Intravesical therapy		MMC single dose	189 (73)	EORTC recurrence score		0	38 (14.7)	Median 72 months, range 12-99	Recurrence Progression	NA – validation of EORTC rates of progression and recurrence	
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Park 2009 1989-2005 South Korea	N=144 84% M/ 16% F Median age 63 yrs All T1G3 undergoing surveillance, 119 (82.6%) treated with IVT after TUR: 115 BCG, 2 MMC, 2 epirubicin. IVT 2 wks after TUR and maintenance BCG not given except in 3 patients	<table border="1"> <tr><td colspan="2">Tumour size</td></tr> <tr><td><3cm</td><td>92 (63.9)</td></tr> <tr><td>≥3cm</td><td>52 (36.1)</td></tr> <tr><td colspan="2">Concomitant CIS</td></tr> <tr><td>Yes</td><td>17 (11.8)</td></tr> <tr><td>No</td><td>127 (88.2)</td></tr> <tr><td colspan="2">Multiplicity</td></tr> <tr><td>Single</td><td>56 (38.9)</td></tr> <tr><td>Multiple</td><td>88 (61.1)</td></tr> <tr><td colspan="2">Lymphovascular invasion</td></tr> <tr><td>Yes</td><td>9 (6.3)</td></tr> <tr><td>No</td><td>135 (93.8)</td></tr> <tr><td colspan="2">Intravesical therapy</td></tr> <tr><td>No</td><td>25 (17.4)</td></tr> <tr><td>Yes</td><td>119 (82.6)</td></tr> <tr><td colspan="2">Gross morphology</td></tr> <tr><td>Papillary</td><td>85 (59)</td></tr> <tr><td>Non-papillary</td><td>59 (41)</td></tr> <tr><td colspan="2">Microscopic morphology</td></tr> <tr><td>Papillary</td><td>93 (64.6)</td></tr> <tr><td>Non-papillary</td><td>51 (35.4)</td></tr> <tr><td colspan="2">Proper muscle</td></tr> <tr><td>Present</td><td>106 (73.6)</td></tr> <tr><td>Absent</td><td>38 (26.4)</td></tr> </table>	Tumour size		<3cm	92 (63.9)	≥3cm	52 (36.1)	Concomitant CIS		Yes	17 (11.8)	No	127 (88.2)	Multiplicity		Single	56 (38.9)	Multiple	88 (61.1)	Lymphovascular invasion		Yes	9 (6.3)	No	135 (93.8)	Intravesical therapy		No	25 (17.4)	Yes	119 (82.6)	Gross morphology		Papillary	85 (59)	Non-papillary	59 (41)	Microscopic morphology		Papillary	93 (64.6)	Non-papillary	51 (35.4)	Proper muscle		Present	106 (73.6)	Absent	38 (26.4)	Median 52.5 mo	Recurrence Progression		
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Alkibay 2009 2002-2006 Turkey	N=6 with micro papillary pattern (MPP), n= 125 without MPP. Treated according to	Patient characteristics not reported separately for NMIBC and MIBC	Median=27.2 mo (12-72)	Progression	Micropapillary pattern (absent or present) -the extent of micropapillary morphology was determined as a tumour percentage																																																	

Study	N patients	Patient Characteristics	Follow-up	Outcomes	Prognostic factors	Comments																																								
	EAU guidelines Mean age 64 years (24-93)																																													
Tilki 2012 1984-2003 USA	N=101 clinical or pathologic stage T1 without nodal mets treated with RC with bilateral lymphadenectomy	<table border="1"> <tr> <td></td> <td>N (%)</td> </tr> <tr> <td>Male</td> <td>86 (85)</td> </tr> <tr> <td>Female</td> <td>15 (15)</td> </tr> <tr> <td colspan="2">Clinical stage (pre RC)</td> </tr> <tr> <td>Ta</td> <td>5 (5)</td> </tr> <tr> <td>Tis</td> <td>5 (5)</td> </tr> <tr> <td>T1</td> <td>91 (90)</td> </tr> <tr> <td colspan="2">Post RC pathological stage</td> </tr> <tr> <td>T0</td> <td>17 (17)</td> </tr> <tr> <td>Ta</td> <td>6 (6)</td> </tr> <tr> <td>Tis</td> <td>21 (21)</td> </tr> <tr> <td>T1</td> <td>57 (56)</td> </tr> <tr> <td colspan="2">Grade (higher of pre-RC and post-RC)</td> </tr> <tr> <td>2</td> <td>10 (10)</td> </tr> <tr> <td>3</td> <td>91 (90)</td> </tr> <tr> <td>Concomitant CIS on RC</td> <td>63 (62)</td> </tr> <tr> <td>Prostate involvement</td> <td>10 (12)</td> </tr> <tr> <td colspan="2">LVI (n=97)</td> </tr> <tr> <td>Yes</td> <td>6 (6)</td> </tr> <tr> <td>No</td> <td>91 (94)</td> </tr> </table>		N (%)	Male	86 (85)	Female	15 (15)	Clinical stage (pre RC)		Ta	5 (5)	Tis	5 (5)	T1	91 (90)	Post RC pathological stage		T0	17 (17)	Ta	6 (6)	Tis	21 (21)	T1	57 (56)	Grade (higher of pre-RC and post-RC)		2	10 (10)	3	91 (90)	Concomitant CIS on RC	63 (62)	Prostate involvement	10 (12)	LVI (n=97)		Yes	6 (6)	No	91 (94)	Median 38 (IQR 22-77) months for patients alive at last visit.	Recurrence-free survival. 4/6 patients with LVI experiences disease recurrence. Disease recurred in 12 patients (all who had LVI or CIS on RC) Cancer-specific survival: 3/6 patients who had LVI died from bladder cancer. All 7 cancer-specific deaths occurred in patients who had concomitant CIS or LVI.	LVI defined as presence of tumour cells within endothelium lined space without underlying muscular walls.	Retrospective study. Low number of patients with LVI. Low number of events
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Branchereau 2013 1994-2009 France	N=108 high grade bladder cancer pT1.	<table border="1"> <tr> <td>Mean age</td> <td>69.1 ±13.1y</td> </tr> <tr> <td>Male</td> <td>81 (87%)</td> </tr> <tr> <td>History of NMIBC</td> <td>20 (19%)</td> </tr> <tr> <td>History of CIS</td> <td>17 (16%)</td> </tr> <tr> <td>Unifocal</td> <td>56%</td> </tr> <tr> <td>Multifocal</td> <td>44%</td> </tr> <tr> <td>Diameter <3cm</td> <td>72%</td> </tr> <tr> <td>pT1a</td> <td>64%</td> </tr> <tr> <td>pT1b</td> <td>36%</td> </tr> </table>	Mean age	69.1 ±13.1y	Male	81 (87%)	History of NMIBC	20 (19%)	History of CIS	17 (16%)	Unifocal	56%	Multifocal	44%	Diameter <3cm	72%	pT1a	64%	pT1b	36%	Mean follow-up 47.8 ±41.2 months	Overall survival	LVI defined as presence of tumour cells within a space limited the endothelium surrounded by a layer of smooth muscle cells. Assessed on the first TURBT.	Retrospective study. Hazard ratios not reported.																						
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Study	N patients	Patient Characteristics		Follow-up	Outcomes	Prognostic factors	Comments
		LVI	39 (36%)				
		Cystectomy	19 (18%)				
Xylinas 2013 2000-2007 Multicentre	N=4689 patients who underwent TURBT for NMIBC. Pure Tis excluded. Re-resection at surgeons discretion within 2-6 weeks. 51% had immediate single postoperative chemotherapy (MMC). All BCG patients were proposed some form of maintenance (at least 1 yr). None had UTUC.		N (%)	Median 46 months for those without recurrence and 57 months for those without progression.	Recurrence – first relapse in bladder regardless of stage Progression – tumour relapse at stage T2 or higher in bladder or prostatic urethra.	EORTC scoring system and CUETO risk tables.	Retrospective study.
		Median age	67 (59-74)				
		male	3721 (79)				
		female	968 (21)				
		Primary	3284 (70)				
		Recurrent	1405 (30)				
		≤1 recurrence/year	727 (16)				
		1 tumour	2865 (61)				
		2-7 tumours	1816 (39)				
		≥8 tumours	8 (<1)				
		<3cm diameter	3698 (79)				
		≥3cm	991 (21)				
		Ta	3030 (65)				
		T1	1659 (35)				
		G1	1419 (30)				
G2	1428 (30)						
G3	1842 (39)						
Concomitant CIS	223 (5)						
Adjuvant BCG	538 (11)						
Xu 2013 2003-2010 China	N=363 patients who underwent TUR for primary and recurrent NMIBC. Primary CIS, nonurothelial cancer, peri-operative radiotherapy, and systemic chemotherapy or cystectomy after TURBT excluded. Re-TUR in high risk patients. No BCG. Immediate adjuvant intravesical chemotherapy in all but		N (%)	Median 36 months (range 4-115)	Recurrence (rate 45.5%) within median 14 months. Progression to MIBC (5.8%)	EORTC scoring system and CUETO risk tables. Recurrence : Low risk 19%; low-intermediate risk 44%; intermediate-high risk 34%; high risk 3% Progression: Low risk 24%; low-intermediate risk 52%; intermediate-high risk 19%; high risk 5%	Retrospective study. Few progression events.
		Mean age	66.1				
		male	265(73)				
		female	98 (27)				
		Primary	212 (58)				
		Recurrent	151 (42)				
		≤1 recurrence/year	36 (9.9)				
		1 tumour	184 (51)				
		2-7 tumours	172 (47)				
		≥8 tumours	7 (2)				
		<3cm diameter	339 (93)				
		≥3cm	24 (7)				
		Ta	273 (75)				
		T1	90 (25)				
		G1	153 (42)				

Study	N patients	Patient Characteristics	Follow-up	Outcomes	Prognostic factors	Comments																																						
	77 patients. Additional chemo 7-15 days after resection (epirubicin or pirarubicin) for 8 weeks with additional monthly maintenance	<table border="1"> <tr> <td>G2</td> <td>159 (44)</td> </tr> <tr> <td>G3</td> <td>51 (14)</td> </tr> <tr> <td>Concomitant CIS</td> <td>11 (3)</td> </tr> </table>	G2	159 (44)	G3	51 (14)	Concomitant CIS	11 (3)																																				
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Olsson 2013 1992-2001 Sweden Retrospective	211 with primary stage T1 UCB. No routine random biopsy, early re-resection in 31 patients. 51 had BCG or chemotherapy. 6 RC and 6 RT	Median age 74y 17% female 80% had recurrence, 39% progression. 32% died from bladder cancer. 25 had concomitant CIS LVI invasion (n=16, 7.5%)	Median 60 months (range 3 to 192 months)	Recurrence Progression Death from bladder cancer.	LVI assessed on the routinely stained histological slides: LVI present/LVI suspected and LVI not present. LVI defined as tumour cells within or attached to the wall of a vascular space.	Retrospective study. Few patients with LVI (n=16).																																						
Lammers 2014 Netherlands 1987-2010 Patient data retrospectively reviewed from prospective studies	728 patients from 3 Dutch studies including patients treated with complete TURBT and adjuvant intravesical epirubicin (n=518) or MMC (n=210).	<table border="1"> <tr> <td></td> <td>N (%)</td> </tr> <tr> <td>Male</td> <td>600 (83)</td> </tr> <tr> <td>Female</td> <td>127 (18)</td> </tr> <tr> <td>Median age</td> <td>68.3 (33-86)</td> </tr> <tr> <td>Primary</td> <td>381 (52)</td> </tr> <tr> <td>Recurrent</td> <td>347 (48)</td> </tr> <tr> <td>History of CIS</td> <td>7 (1)</td> </tr> <tr> <td>Previous treatment</td> <td>619 (86)</td> </tr> <tr> <td>Ta</td> <td>568 (78)</td> </tr> <tr> <td>T1</td> <td>160 (22)</td> </tr> <tr> <td>G1</td> <td>294 (40)</td> </tr> <tr> <td>G2</td> <td>346 (48)</td> </tr> <tr> <td>G3</td> <td>88 (12)</td> </tr> <tr> <td>Single</td> <td>184 (25)</td> </tr> <tr> <td><3cm</td> <td>574 (79)</td> </tr> <tr> <td>EUA low risk recurrence</td> <td>1 (0.1)</td> </tr> <tr> <td>EUA intermediate recurrence</td> <td>668 (92)</td> </tr> <tr> <td>EUA high recurrence</td> <td>59 (8)</td> </tr> <tr> <td>EUA low risk progression</td> <td>19 (3)</td> </tr> </table>		N (%)	Male	600 (83)	Female	127 (18)	Median age	68.3 (33-86)	Primary	381 (52)	Recurrent	347 (48)	History of CIS	7 (1)	Previous treatment	619 (86)	Ta	568 (78)	T1	160 (22)	G1	294 (40)	G2	346 (48)	G3	88 (12)	Single	184 (25)	<3cm	574 (79)	EUA low risk recurrence	1 (0.1)	EUA intermediate recurrence	668 (92)	EUA high recurrence	59 (8)	EUA low risk progression	19 (3)	Median follow-up 28.2 months (2-76)	Recurrence Progression	EORTC scoring system used to reclassify patients. Observed recurrence and progression compared against those predicted from EORTC	317 patients with missing data
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Study	N patients	Patient Characteristics		Follow-up	Outcomes	Prognostic factors	Comments
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		EAU high progression	185 (25)				