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Supplementary material

Radical Cystectomy against intra-vesical BCG immunotherapy for high-risk high grade non-muscle invasive bladder cancer: Results from the randomised controlled BRAVO-feasibility study

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Study Registration: ISRCTN12509361 Registered 06/09/16.

Supp Table 1. Characteristics of the screened and randomised population and reasons for ineligibility

	Screened	Randomised
Total	407 (100%)	50 (100%)
Patient Sex		
Male	315 (77.4%)	41 (82.0%)
Female	92 (22.6%)	9 (18.0%)
Age category		
< 40	2 (0.5%)	0 (0.0%)
40 - 49	1 (0.2%)	0 (0.0%)
50 - 59	35 (8.6%)	4 (8.0%)
60 - 69	102 (25.1%)	19 (38.0%)
70 -79	186 (45.7%)	22 (44.0%)
≥80	81 (19.9%)	5 (10.0%)
Place patient presented		
District general hospital	177 (43.5%)	
Cancer centre	230 (56.5%)	
Patient considered for BRAVO		
Yes	215 (52.8%)	
No	192 (47.2%)	
Reason not considered		
Patient ineligible	187 (94.9%)	
Clinician choice	5 (2.5%)	
Patient preference	2 (1.0%)	
Other	3 (1.5%)	
Reasons for ineligibility		
Does not have new HRNMIBC	20 (8.8%)	
Previous HRNMIBC	30 (13.3%)	
Prior treatment with intravesical BCG	14 (6.2%)	
Prior pelvic radiotherapy	8 (3.5%)	
Tumour in bladder diverticulum	1 (0.4%)	
Tumour not UCC or UCC as majority	4 (1.8%)	
No additional risk factors	42 (18.6%)	
Incomplete imaging	2 (0.8%)	
Not suitable for BCG & RC	71 (31.4%)	
Has had another malignancy	31 (13.7%)	
Unable/unwilling to give informed consent	3 (1.3%)	
Stage in pathway		
After initial TURBT	118 (29.0%)	
After local MDT	40 (9.8%)	
Before re-resection	17 (4.2%)	
After re-resection	37 (9.1%)	
After specialist MDT	188 (46.2%)	
Direct contact initiated by patient	0 (0.0%)	
Other	7 (1.7%)	

Supp Table 2. Occupational details and additional baseline characteristics for randomised patients

	Radical Cystectomy	BCG immunotherapy	Total
Industries worked in - not mutually exclusive			
Rubber/plastic manufacture	1 (3.4%)	1 (4.0%)	2 (3.7%)
Dye/paint industry	2 (6.9%)	1 (4.0%)	3 (5.6%)
Petrochemical industry	0 (0.0%)	1 (4.0%)	1 (1.9%)
Driver/transport industry	7 (24.1%)	2 (8.0%)	9 (16.7%)
Metal manufacture/machine setter/operator	4 (13.8%)	8 (32.0%)	12 (22.2%)
Leather worker/textiles industry	2 (6.9%)	1 (4.0%)	3 (5.6%)
Printing	0 (0.0%)	0 (0.0%)	0 (0.0%)
Mechanic/automobile industry	0 (0.0%)	1 (4.0%)	1 (1.9%)
Hairdressers	1 (3.4%)	1 (4.0%)	2 (3.7%)
Other	12 (41.4%)	9 (36.0%)	21 (38.9%)
Taking part in other clinical trials?			
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)
No	25 (100.0%)	24 (96.0%)	49 (98.0%)
Missing	0 (0.0%)	1 (4.0%)	1 (2.0%)
Previous treatment for low risk bladder cancer			
Yes	2 (8.0%)	1 (4.0%)	3 (6.0%)
No	23 (92.0%)	24 (96.0%)	47 (94.0%)
ASA status			
I - A normal healthy patient	12 (48.0%)	12 (48.0%)	24 (48.0%)
II - A patient with mild systematic disease	12 (48.0%)	11 (44.0%)	23 (46.0%)
III - A patient with severe systemic disease	1 (4.0%)	1 (4.0%)	2 (4.0%)
IV - A patient with severe systemic disease that is a constant threat to life	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	1 (4.0%)	1 (2.0%)
Number of flexible cystoscopies			
0	4 (16.0%)	3 (12.0%)	7 (14.0%)
1	20 (80.0%)	21 (84.0%)	41 (82.0%)
2	1 (4.0%)	0 (0.0%)	1 (2.0%)
Missing	0 (0.0%)	1 (4.0%)	1 (2.0%)
Number of rigid cystoscopies			
0	1 (4.0%)	0 (0.0%)	1 (2.0%)
1	8 (32.0%)	5 (20.0%)	13 (26.0%)
2	13 (52.0%)	16 (64.0%)	29 (58.0%)
3	2 (8.0%)	4 (16.0%)	6 (12.0%)
4	0 (0.0%)	0 (0.0%)	0 (0.0%)
5	1 (4.0%)	0 (0.0%)	1 (2.0%)
Anaesthetic assessment to confirm RC eligibility			
Yes	6 (24.0%)	4 (16.0%)	10 (20.0%)
No	12 (48.0%)	11 (44.0%)	23 (46.0%)
N/A	7 (28.0%)	9 (36.0%)	16 (32.0%)
Missing	0 (0.0%)	1 (4.0%)	1 (2.0%)
Imaging for suspicion of metastatic disease			
Yes	3 (12.0%)	0 (0.0%)	3 (6.0%)
No / NA	22 (88.0%)	24 (96.0%)	46 (92.0%)
Missing	0 (0.0%)	1 (4.0%)	1 (2.0%)
Serum creatinine, by arm			
Mean (s.d.)	81.2 (17.68)	89.1 (23.63)	85.1 (20.97)
Median (range)	78.0 (44.0, 114.0)	87.5 (57.0, 170.0)	83.0 (44.0, 170.0)
Missing	0	1	1

Supp Table 3. Adverse events

	BCG Cycle 1	BCG Cycle 2	BCG Cycle 3	Radical Cystectomy	
General Disorders and Administrative Site Conditions					
Chills	0 (0.0%)	1 (6.7%)			
Fever	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Malaise	2 (5.9%)	2 (13.3%)	0 (0.0%)		
Infection and Infestation					
Urinary Tract Infection	2 (5.9%)	0 (0.0%)	0 (0.0%)		
Metabolism and Nutrition Disorders					
Anorexia	1 (2.9%)	0 (0.0%)	0 (0.0%)		
Musculoskeletal, Connective Tissue and Bone Disorders					
Arthralgia	0 (0.0%)	0 (0.0%)	0 (0.0%)		
Myalgia	1 (2.9%)	2 (13.3%)	0 (0.0%)		
Renal and Urinary Disorders					
Bladder cramps/pain	1 (2.9%)	0 (0.0%)	0 (0.0%)		
Dysuria	8 (23.5%)	4 (26.7%)	1 (50.0%)		
Haematuria	2 (5.9%)	0 (0.0%)	0 (0.0%)		
Urinary frequency	10 (29.4%)	4 (26.7%)	1 (50.0%)		
Urinary incontinence	2 (5.9%)	0 (0.0%)	0 (0.0%)		
Urinary urgency	4 (11.8%)	1 (6.7%)	0 (0.0%)		
Skin and Subcutaneous Tissues Disorders					
Skin rash	1 (2.9%)	1 (6.7%)	0 (0.0%)		
Intra-operative					
Haemorrhage/bleeding				2 (40.0%)	
Small bowel injury				1 (20.0%)	
Nerve injury				1 (20.0%)	
Difficult dissection				1 (20.0%)	
Post-operative					
Chest infection				3 (33.3%)	
Wound infection				1 (11.1%)	
Prolonged ileus				3 (33.3%)	
Urine leak				1 (11.1%)	
Constipation				1 (11.1%)	
Total	34 (100%)	15 (100%)	2 (100%)	5 (100%)	9 (100%)

Supp Table 4. EQ-5D-3L

	Baseline			3 months post-randomisation			6 months post-randomisation			12 months post-randomisation		
	RC	mBCG	Total	RC	mBCG	Total	RC	mBCG	Total	RC	mBCG	Total
Mobility												
I have no problems in walking about	18 (72.0%)	19 (79.2%)	37 (75.5%)	13 (76.5%)	14 (63.6%)	27 (69.2%)	11 (61.1%)	15 (78.9%)	26 (70.3%)	11 (78.6%)	10 (62.5%)	21 (70.0%)
I have some problems in walking about	6 (24.0%)	5 (20.8%)	11 (22.4%)	4 (23.5%)	8 (36.4%)	12 (30.8%)	6 (33.3%)	3 (15.8%)	9 (24.3%)	3 (21.4%)	6 (37.5%)	9 (30.0%)
I am confined to bed	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	1 (4.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.3%)	2 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	25 (100%)	24 (100%)	49 (100%)	17 (100%)	22 (100%)	39 (100%)	18 (100%)	19 (100%)	37 (100%)	14 (100%)	16 (100%)	30 (100%)
Self-care												
I have no problems with self-care	22 (88.0%)	23 (95.8%)	45 (91.8%)	15 (88.2%)	20 (90.9%)	35 (89.7%)	14 (77.8%)	18 (94.7%)	32 (86.5%)	12 (85.7%)	15 (93.8%)	27 (90.0%)
I have some problems washing or dressing myself	3 (12.0%)	1 (4.2%)	4 (8.2%)	2 (11.8%)	2 (9.1%)	4 (10.3%)	3 (16.7%)	0 (0.0%)	3 (8.1%)	2 (14.3%)	1 (6.3%)	3 (10.0%)
I am unable to wash or dress myself	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.3%)	2 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	25 (100%)	24 (100%)	49 (100%)	17 (100%)	22 (100%)	39 (100%)	18 (100%)	19 (100%)	37 (100%)	14 (100%)	16 (100%)	30 (100%)
Usual activities												
I have no problems with performing my usual activities	20 (80.0%)	21 (87.5%)	41 (83.7%)	7 (41.2%)	16 (72.7%)	23 (59.0%)	10 (55.6%)	12 (63.2%)	22 (59.5%)	10 (71.4%)	9 (56.3%)	19 (63.3%)
I have some problems with performing my usual activities	3 (12.0%)	3 (12.5%)	6 (12.2%)	9 (52.9%)	5 (22.7%)	14 (35.9%)	6 (33.3%)	6 (31.6%)	12 (32.4%)	4 (28.6%)	7 (43.8%)	11 (36.7%)
I am unable to perform my usual activities	1 (4.0%)	0 (0.0%)	1 (2.0%)	1 (5.9%)	1 (4.5%)	2 (5.1%)	1 (5.6%)	0 (0.0%)	1 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	1 (4.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.3%)	2 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	25 (100%)	24 (100%)	49 (100%)	17 (100%)	22 (100%)	39 (100%)	18 (100%)	19 (100%)	37 (100%)	14 (100%)	16 (100%)	30 (100%)
Pain/Discomfort												
I have no pain or discomfort	12 (48.0%)	14 (58.3%)	26 (53.1%)	8 (47.1%)	14 (63.6%)	22 (56.4%)	7 (38.9%)	12 (63.2%)	19 (51.4%)	10 (71.4%)	8 (50.0%)	18 (60.0%)
I have moderate pain or discomfort	12 (48.0%)	9 (37.5%)	21 (42.9%)	9 (52.9%)	7 (31.8%)	16 (41.0%)	10 (55.6%)	6 (31.6%)	16 (43.2%)	4 (28.6%)	8 (50.0%)	12 (40.0%)
I have extreme pain or discomfort	1 (4.0%)	1 (4.2%)	2 (4.1%)	0 (0.0%)	1 (4.5%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.3%)	2 (5.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total	25 (100%)	24 (100%)	49 (100%)	17 (100%)	22 (100%)	39 (100%)	18 (100%)	19 (100%)	37 (100%)	14 (100%)	16 (100%)	30 (100%)
Anxiety/Depression												
I am not anxious or depressed	18 (72.0%)	18 (75.0%)	36 (73.5%)	11 (64.7%)	15 (68.2%)	26 (66.7%)	11 (61.1%)	13 (68.4%)	24 (64.9%)	12 (85.7%)	11 (68.8%)	23 (76.7%)
I am moderately anxious or depressed	7 (28.0%)	4 (16.7%)	11 (22.4%)	6 (35.3%)	6 (27.3%)	12 (30.8%)	6 (33.3%)	5 (26.3%)	11 (29.7%)	1 (7.1%)	3 (18.8%)	4 (13.3%)
I am extremely anxious or depressed	0 (0.0%)	1 (4.2%)	1 (2.0%)	0 (0.0%)	1 (4.5%)	1 (2.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (7.1%)	1 (6.3%)	2 (6.7%)
Missing	0 (0.0%)	1 (4.2%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (5.6%)	1 (5.3%)	2 (5.4%)	0 (0.0%)	1 (6.3%)	1 (3.3%)
Total	25 (100%)	24 (100%)	49 (100%)	17 (100%)	22 (100%)	39 (100%)	18 (100%)	19 (100%)	37 (100%)	14 (100%)	16 (100%)	30 (100%)
Indicate your health today (scale)												
Mean (s.d.)	76.8 (18.2)	79.0 (17.2)	77.9 (17.5)	74.9 (12.6)	73.1 (23.3)	73.9 (19.3)	74.6 (16.4)	78.1 (18.2)	76.3 (17.1)	80.1 (25.6)	77.6 (14.8)	78.7 (20.0)
Median (range)	80 (22, 100)	83 (30, 99)	80 (22, 100)	70 (50, 90)	75 (2, 95)	75 (2, 95)	75 (40, 100)	82 (40, 100)	80 (40, 100)	90 (7, 100)	80 (39, 95)	80 (7, 100)
Missing	2	2	4	2	1	3	0	2	2	1	0	1
N	23	22	45	15	21	36	18	17	35	13	16	29
EQ-5D-3L Score												
Mean (s.d.)	0.8 (0.18)	0.8 (0.24)	0.8 (0.21)	0.8 (0.16)	0.8 (0.30)	0.8 (0.24)	0.8 (0.17)	0.9 (0.16)	0.8 (0.17)	0.9 (0.22)	0.8 (0.22)	0.8 (0.22)
Median (range)	1 (0, 1)	1 (0, 1)	1 (0, 1)	1 (0, 1)	1 (0, 1)	1 (-0, 1)	1 (0, 1)	1 (1, 1)	1 (0, 1)	1 (0, 1)	1 (0, 1)	1 (0, 1)
Missing	2	1	3	0	0	0	1	1	2	0	1	1
N	23	23	46	17	22	39	17	18	35	14	15	29

Supp Table 5. QLQ-C30

	Baseline			3 months post-randomisation			6 months post-randomisation			12 months post-randomisation		
	RC	mBCG	Total	RC	mBCG	Total	RC	mBCG	Total	RC	mBCG	Total
Functional scales												
Physical functioning												
Mean (s.d.)	90.4 (14.0)	83.6 (21.9)	87.1 (18.4)	72.5 (22.5)	79.6 (20.2)	76.3 (21.3)	82.1 (19.0)	80.4 (19.1)	81.2 (18.7)	84.8 (18.9)	84.0 (16.5)	84.4 (17.4)
Median (range)	93 (40, 100)	93 (27, 100)	93 (27, 100)	80 (33, 100)	80 (27, 100)	80 (27, 100)	87 (47, 100)	87 (53, 100)	87 (47, 100)	90 (40, 100)	87 (53, 100)	87 (40, 100)
Missing	0	0	0	0	3	3	2	2	4	0	1	1
N	25	24	49	17	19	36	16	17	33	14	15	29
Role functioning												
Mean (s.d.)	88.0 (19.0)	81.2 (31.6)	84.7 (25.9)	69.6 (27.8)	76.3 (32.1)	73.1 (29.9)	74.1 (37.6)	77.8 (23.6)	75.9 (31.0)	83.3 (28.5)	77.1 (22.7)	80.0 (25.3)
Median (range)	100 (33, 100)	100 (0, 100)	100 (0, 100)	67 (33, 100)	100 (17, 100)	83 (17, 100)	100 (0, 100)	75 (33, 100)	100 (0, 100)	100 (33, 100)	67 (33, 100)	100 (33, 100)
Missing	0	0	0	0	3	3	0	1	1	0	0	0
N	25	24	49	17	19	36	18	18	36	14	16	30
Emotional functioning												
Mean (s.d.)	82.6 (22.3)	79.7 (19.9)	81.2 (21.0)	75.5 (29.3)	83.3 (15.8)	79.9 (22.7)	83.8 (24.7)	85.2 (15.3)	84.5 (20.2)	86.9 (28.1)	81.7 (17.0)	84.2 (22.8)
Median (range)	92 (0, 100)	83 (25, 100)	88 (0, 100)	92 (0, 100)	83 (42, 100)	88 (0, 100)	92 (0, 100)	92 (58, 100)	92 (0, 100)	100 (0, 100)	83 (42, 100)	92 (0, 100)
Missing	2	1	3	1	2	3	0	1	1	0	1	1
N	23	23	46	16	20	36	18	18	36	14	15	29
Cognitive functioning												
Mean (s.d.)	93.5 (10.9)	86.1 (23.4)	89.7 (18.6)	89.2 (14.4)	90.0 (13.7)	89.6 (13.8)	90.2 (18.7)	95.4 (7.68)	92.9 (14.2)	89.7 (14.5)	94.4 (10.3)	92.3 (12.4)
Median (range)	100 (67, 100)	100 (0, 100)	100 (0, 100)	100 (50, 100)	100 (67, 100)	100 (50, 100)	100 (33, 100)	100 (83, 100)	100 (33, 100)	100 (67, 100)	100 (67, 100)	100 (67, 100)
Missing	2	0	2	0	2	2	1	1	2	1	1	2
N	23	24	47	17	20	37	17	18	35	13	15	28
Social functioning												
Mean (s.d.)	92.4 (12.0)	81.9 (23.5)	87.2 (19.2)	77.1 (22.7)	76.7 (27.8)	76.9 (25.3)	72.2 (28.6)	83.3 (18.1)	77.8 (24.2)	83.3 (25.6)	82.2 (16.0)	82.7 (20.4)
Median (range)	100 (67, 100)	92 (17, 100)	100 (17, 100)	67 (33, 100)	83 (17, 100)	83 (17, 100)	75 (17, 100)	92 (50, 100)	83 (17, 100)	100 (17, 100)	83 (67, 100)	83 (17, 100)
Missing	1	0	1	1	2	3	0	1	1	2	1	3
N	24	24	48	16	20	36	18	18	36	12	15	27
Symptom scales / items												
Fatigue												
Mean (s.d.)	18.1 (19.9)	24.1 (26.6)	21.1 (23.4)	30.1 (19.2)	25.9 (29.3)	27.9 (24.6)	26.5 (24.1)	25.0 (21.3)	25.8 (22.5)	22.2 (28.2)	19.0 (13.4)	20.6 (21.7)
Median (range)	11 (0, 78)	22 (0, 100)	11 (0, 100)	22 (0, 89)	22 (0, 89)	22 (0, 89)	22 (0, 67)	33 (0, 67)	28 (0, 67)	17 (0, 100)	17 (0, 44)	17 (0, 100)
Missing	1	0	1	0	4	4	0	3	3	0	2	2
N	24	24	48	17	18	35	18	16	34	14	14	28
Nausea and vomiting												
Mean (s.d.)	2.7 (6.24)	0.7 (3.40)	1.7 (5.10)	5.2 (10.0)	2.6 (6.24)	3.8 (8.17)	2.8 (8.57)	4.6 (9.58)	3.7 (9.01)	3.6 (7.10)	1.2 (4.45)	2.4 (5.94)
Median (range)	0 (0, 17)	0 (0, 17)	0 (0, 17)	0 (0, 33)	0 (0, 17)	0 (0, 33)	0 (0, 33)	0 (0, 33)	0 (0, 33)	0 (0, 17)	0 (0, 17)	0 (0, 17)
Missing	0	0	0	1	3	4	0	1	1	0	2	2
N	25	24	49	16	19	35	18	18	36	14	14	28
Pain												
Mean (s.d.)	15.3 (16.2)	13.9 (22.9)	14.6 (19.6)	24.5 (15.7)	21.3 (27.9)	22.9 (22.5)	20.4 (27.7)	17.6 (19.1)	19.0 (23.6)	10.3 (12.8)	14.4 (16.5)	12.5 (14.8)
Median (range)	17 (0, 50)	0 (0, 100)	8 (0, 100)	33 (0, 50)	17 (0, 100)	17 (0, 100)	8 (0, 83)	17 (0, 50)	17 (0, 83)	0 (0, 33)	0 (0, 33)	0 (0, 33)
Missing	1	0	1	0	4	4	0	2	2	1	1	2
N	24	24	48	17	18	35	18	17	35	13	15	28
Dyspnoea												
Mean (s.d.)	8.0 (14.5)	11.1 (18.8)	9.5 (16.7)	14.6 (21.0)	15.8 (28.0)	15.2 (24.7)	13.0 (20.3)	7.4 (14.3)	10.2 (17.5)	11.9 (21.1)	12.5 (20.6)	12.2 (20.5)
Median (range)	0 (0, 33)	0 (0, 67)	0 (0, 67)	0 (0, 67)	0 (0, 100)	0 (0, 100)	0 (0, 67)	0 (0, 33)	0 (0, 67)	0 (0, 67)	0 (0, 67)	0 (0, 67)
Missing	0	0	0	1	3	4	0	1	1	0	0	0
N	25	24	49	16	19	35	18	18	36	14	16	30
Insomnia												
Mean (s.d.)	33.3 (33.3)	26.4 (36.8)	29.9 (34.9)	17.6 (23.9)	31.6 (28.3)	25.0 (26.9)	27.8 (36.6)	31.5 (33.3)	29.6 (34.5)	21.4 (31.0)	33.3 (32.2)	27.8 (31.7)
Median (range)	33 (0, 100)	0 (0, 100)	33 (0, 100)	0 (0, 67)	33 (0, 67)	33 (0, 67)	17 (0, 100)	33 (0, 100)	33 (0, 100)	0 (0, 100)	33 (0, 100)	33 (0, 100)
Missing	0	0	0	0	3	3	0	1	1	0	0	0
N	25	24	49	17	19	36	18	18	36	14	16	30
Appetite loss												
Mean (s.d.)	6.7 (16.7)	9.7 (18.3)	8.2 (17.4)	7.8 (14.6)	8.8 (15.1)	8.3 (14.6)	13.0 (28.3)	11.1 (16.2)	12.0 (22.8)	7.1 (14.2)	9.5 (15.6)	8.3 (14.7)
Median (range)	0 (0, 67)	0 (0, 67)	0 (0, 67)	0 (0, 33)	0 (0, 33)	0 (0, 33)	0 (0, 100)	0 (0, 33)	0 (0, 100)	0 (0, 33)	0 (0, 33)	0 (0, 33)
Missing	0	0	0	0	3	3	0	1	1	0	2	2
N	25	24	49	17	19	36	18	18	36	14	14	28
Constipation												
Mean (s.d.)	4.0 (11.1)	6.9 (19.6)	5.4 (15.7)	27.1 (34.9)	8.8 (15.1)	17.1 (27.3)	11.8 (16.4)	16.7 (20.6)	14.3 (18.6)	7.1 (14.2)	16.7 (21.1)	12.2 (18.5)
Median (range)	0 (0, 33)	0 (0, 67)	0 (0, 67)	17 (0, 100)	0 (0, 33)	0 (0, 100)	0 (0, 33)	0 (0, 67)	0 (0, 67)	0 (0, 33)	0 (0, 67)	0 (0, 67)
Missing	0	0	0	1	3	4	1	1	2	0	0	0
N	25	24	49	16	19	35	17	18	35	14	16	30
Diarrhoea												
Mean (s.d.)	2.8 (9.41)	4.2 (11.3)	3.5 (10.3)	7.8 (18.7)	4.8 (15.9)	6.1 (17.1)	9.3 (19.2)	5.6 (12.8)	7.4 (16.2)	9.5 (20.4)	2.2 (8.61)	5.7 (15.6)
Median (range)	0 (0, 33)	0 (0, 33)	0 (0, 33)	0 (0, 67)	0 (0, 67)	0 (0, 67)	0 (0, 67)	0 (0, 33)	0 (0, 67)	0 (0, 67)	0 (0, 33)	0 (0, 67)
Missing	1	0	1	0	1	1	0	1	1	0	1	1
N	24	24	48	17	21	38	18	18	36	14	15	29
Financial difficulties												
Mean (s.d.)	8.3 (22.5)	9.7 (20.8)	9.0 (21.5)	6.3 (25.0)	9.5 (23.9)	8.1 (24.1)	14.8 (34.7)	3.7 (10.8)	9.3 (26.0)	7.1 (26.7)	4.4 (11.7)	5.7 (20.1)
Median (range)	0 (0, 100)	0 (0, 67)	0 (0, 100)	0 (0, 100)	0 (0, 100)	0 (0, 100)	0 (0, 100)	0 (0, 33)	0 (0, 100)	0 (0, 100)	0 (0, 33)	0 (0, 100)
Missing	1	1	1	1	1	2	0	1	1	0	1	1
N	24	24	48	16	21	37	18	18	36	14	15	29
Global health status												
Global health status												
Mean (s.d.)	77.1 (16.5)	77.8 (18.7)	77.4 (17.4)	71.6 (15.9)	76.6 (20.5)	74.3 (18.5)	71.8 (19.2)	74.1 (17.1)	72.9 (18.0)	74.4 (22.0)	74.4 (18.5)	74.4 (19.9)
Median (range)	79 (33, 100)	83 (33, 100)	83 (33, 100)	67 (42, 100)	83 (42, 100)	75 (42, 100)	71 (33, 100)	83 (42, 100)	79 (33, 100)	83 (17, 100)	83 (33, 100)	83 (17, 100)
Missing	1	0	1	0	1	1	0	1	1	0	1	1
N	24	24	48	17	21	38	18	18	36	14	15	29

All scores range from 0-100. A high score represents a higher response level. Hence, a high functional scale score represents a healthy level of functioning, a high symptom item/scale score represents a high level of symptomatology and a high global health score represents a high quality of life.

Supp Table 6. QLQ-NMIBC24

	RC	Baseline mBCG	Total	3 months mBCG	6 months mBCG	12 months mBCG
Urinary symptoms scale						
Mean (s.d.)	28.4 (21.5)	25.2 (21.1)	26.8 (21.1)	21.9 (19.9)	29.4 (20.6)	22.6 (23.9)
Median (range)	26 (0, 71)	21 (0, 71)	24 (0, 71)	14 (0, 71)	24 (0, 71)	17 (0, 67)
Missing	1	0	1	2	2	0
N	24	24	48	20	17	16
Malaise scale						
Mean (s.d.)	1.4 (4.71)	4.9 (17.4)	3.1 (12.7)	6.1 (11.0)	5.6 (9.90)	3.1 (6.72)
Median (range)	0 (0, 17)	0 (0, 83)	0 (0, 83)	0 (0, 33)	0 (0, 33)	0 (0, 17)
Missing	1	0	1	0	1	0
N	24	24	48	22	18	16
Future worries scale						
Mean (s.d.)	42.0 (25.9)	44.8 (25.0)	43.4 (25.3)	34.8 (18.7)	27.9 (17.7)	27.8 (16.3)
Median (range)	42 (0, 100)	33 (0, 100)	38 (0, 100)	33 (0, 67)	25 (0, 67)	25 (0, 75)
Missing	1	0	1	0	2	1
N	24	24	48	22	17	15
Bloating and flatulence scale						
Mean (s.d.)	13.9 (15.3)	22.9 (25.9)	18.4 (21.5)	18.2 (17.0)	20.4 (16.7)	26.0 (24.3)
Median (range)	17 (0, 50)	17 (0, 100)	17 (0, 100)	17 (0, 50)	17 (0, 50)	17 (0, 83)
Missing	1	0	1	0	1	0
N	24	24	48	22	18	16
Sexual function scale						
Mean (s.d.)	29.0 (28.5)	9.7 (14.7)	19.1 (24.3)	19.8 (25.6)	17.9 (22.1)	25.0 (29.8)
Median (range)	17 (0, 100)	0 (0, 50)	17 (0, 100)	17 (0, 100)	8 (0, 67)	25 (0, 100)
Missing	2	0	2	1	5	2
N	23	24	47	21	14	14
Male sexual problems						
Mean (s.d.)	20.6 (26.7)	31.6 (40.4)	26.4 (34.6)	25.0 (36.8)	31.7 (38.0)	44.4 (42.5)
Median (range)	17 (0, 100)	0 (0, 100)	8 (0, 100)	8 (0, 100)	17 (0, 100)	17 (0, 100)
Missing	2	2	4	5	6	5
N	17	19	36	14	10	9
Intravesical treatment issues						
Mean (s.d.)	13.0 (26.1)	14.5 (24.3)	13.8 (24.9)	12.1 (19.4)	16.7 (23.6)	12.5 (16.7)
Median (range)	0 (0, 100)	0 (0, 100)	0 (0, 100)	0 (0, 67)	0 (0, 67)	0 (0, 33)
Missing	2	1	3	0	1	0
N	23	23	46	22	18	16
Sexual intimacy						
Mean (s.d.)	4.8 (12.1)	16.7 (32.4)	9.7 (23.0)	23.8 (31.7)	18.5 (24.2)	11.1 (17.2)
Median (range)	0 (0, 33)	0 (0, 100)	0 (0, 100)	0 (0, 67)	0 (0, 67)	0 (0, 33)
Missing	11	14	25	15	10	10
N	14	10	24	7	9	6
Risk of contaminating partner						
Mean (s.d.)	26.2 (35.0)	16.7 (32.4)	22.2 (33.6)	66.7 (43.0)	29.6 (38.9)	22.2 (27.2)
Median (range)	0 (0, 100)	0 (0, 100)	0 (0, 100)	100 (0, 100)	0 (0, 100)	17 (0, 67)
Missing	11	14	25	15	10	10
N	14	10	24	7	9	6
Sexual enjoyment						
Mean (s.d.)	66.7 (41.3)	40.0 (46.6)	55.6 (44.7)	57.1 (37.1)	44.4 (40.8)	61.1 (39.0)
Median (range)	83 (0, 100)	17 (0, 100)	67 (0, 100)	67 (0, 100)	33 (0, 100)	67 (0, 100)
Missing	11	14	25	15	10	10
N	14	10	24	7	9	6
Female sexual problems						
Mean (s.d.)	16.7 (23.6)	0 (0.0%)	11.1 (19.2)	0 (0.0%)	0 (0.0%)	0.0 (.)
Median (range)	17 (0, 33)	0 (0, 0)	0 (0, 33)	0 (0.0%)	0 (0, 0)	0 (0, 0)
Missing	4	2	6	2	2	1
N	2	1	3	1	1	1
Felt less attractive						
Not at All	21 (84.0%)	19 (79.2%)	40 (81.6%)	17 (77.3%)	12 (63.2%)	13 (81.3%)
A Little	3 (12.0%)	4 (16.7%)	7 (14.3%)	3 (13.6%)	5 (26.3%)	2 (12.5%)
Quite a Bit	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.5%)	1 (5.3%)	1 (6.3%)
Very Much	1 (4.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	1 (4.2%)	1 (2.0%)	1 (4.5%)	1 (5.3%)	0 (0.0%)
Total	25 (100%)	24 (100%)	49 (100%)	22 (100%)	19 (100%)	16 (100%)
Dissatisfied with body						
Not at All	21 (84.0%)	15 (62.5%)	36 (73.5%)	15 (68.2%)	9 (47.4%)	11 (68.8%)
A Little	2 (8.0%)	5 (20.8%)	7 (14.3%)	5 (22.7%)	5 (26.3%)	3 (18.8%)
Quite a Bit	0 (0.0%)	3 (12.5%)	3 (6.1%)	1 (4.5%)	3 (15.8%)	2 (12.5%)
Very Much	2 (8.0%)	0 (0.0%)	2 (4.1%)	1 (4.5%)	0 (0.0%)	0 (0.0%)
Missing	0 (0.0%)	1 (4.2%)	1 (2.0%)	0 (0.0%)	2 (10.5%)	0 (0.0%)
Total	25 (100%)	24 (100%)	49 (100%)	22 (100%)	19 (100%)	16 (100%)
Felt less masculine/feminine						
Not at All	22 (88.0%)	19 (79.2%)	41 (83.7%)	18 (81.8%)	12 (63.2%)	12 (75.0%)
A Little	1 (4.0%)	2 (8.3%)	3 (6.1%)	3 (13.6%)	4 (21.1%)	4 (25.0%)
Quite a Bit	1 (4.0%)	2 (8.3%)	3 (6.1%)	1 (4.5%)	1 (5.3%)	0 (0.0%)
Very Much	1 (4.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)
Missing	0 (0.0%)	1 (4.2%)	1 (2.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)
Total	25 (100%)	24 (100%)	49 (100%)	22 (100%)	19 (100%)	16 (100%)

A high score for urinary symptoms, malaise, bloating and flatulence indicate more symptoms. A high score for future worries indicates more worry, a high score for sexual function indicates better functioning and a high score for male sexual problems indicates more problems. Similarly, for individual items intravesical treatment issues, sexual intimacy, risk of contaminating partner and female sexual problems, a high score is interpreted as worse. However, for the individual item sexual enjoyment, a high score is better

Supp Table 7. QLQ-BLM30

	3 months post-randomisation	6 months post-randomisation	12 months post-randomisation
	RC	RC	RC
Urinary symptoms			
Mean (s.d.)	28.6 (6.73)	17.9 (2.38)	9.5 (6.73)
Median (range)	26 (24, 38)	19 (14, 19)	12 (0, 14)
Missing	7	13	9
N	4	4	4
Urostomy problems			
Mean (s.d.)	21.4 (19.6)	17.2 (14.9)	12.3 (18.0)
Median (range)	17 (0, 56)	11 (0, 44)	6 (0, 56)
Missing	4	7	4
N	7	10	9
Future perspective			
Mean (s.d.)	56.6 (30.0)	35.3 (21.2)	24.1 (29.9)
Median (range)	56 (22, 100)	33 (11, 89)	17 (0, 89)
Missing	0	0	1
N	11	17	12
Abdominal bloating and flatulence scale			
Mean (s.d.)	27.3 (26.1)	24.5 (23.7)	25.0 (27.1)
Median (range)	17 (0, 83)	17 (0, 83)	17 (0, 100)
Missing	0	0	1
N	11	17	12
Body image			
Mean (s.d.)	24.2 (20.4)	15.7 (22.9)	18.5 (17.3)
Median (range)	22 (0, 67)	11 (0, 89)	22 (0, 44)
Missing	0	0	1
N	11	17	12
Sexual function scale			
Mean (s.d.)	22.6 (25.4)	32.3 (26.5)	22.0 (22.9)
Median (range)	8 (0, 57)	43 (0, 62)	21 (0, 57)
Missing	2	6	5
N	9	11	8

Scores range from 0 to 100. A high score for urinary symptoms, urostomy problems, future perspective, abdominal bloating and flatulence and body image, represents a high level of symptomatology. A high score for sexual functioning represents a high level of functioning

Supp Table 8. Decision regret responses in participants 12 months after recruitment

Decision regret regarding decision to take part in study

	Radical Cystectomy	BCG immunotherapy	Total
It was the right decision			
Mean (s.d.)	16.2 (12.3)	11.3 (22.2)	13.5 (18.3)
Median (range)	25 (0, 25)	0 (0, 75)	0 (0, 75)
Missing	1	1	2
N	17	20	37
I regret the choice that was made			
Mean (s.d.)	20.6 (20.2)	27.8 (37.3)	24.3 (30.0)
Median (range)	25 (0, 75)	0 (0, 100)	25 (0, 100)
Missing	1	3	4
N	17	18	35
I would go for the same choice if I had to do it over again			
Mean (s.d.)	13.2 (12.9)	10.0 (20.5)	11.5 (17.3)
Median (range)	25 (0, 25)	0 (0, 75)	0 (0, 75)
Missing	1	1	2
N	17	20	37
The choice did me a lot of harm			
Mean (s.d.)	15.6 (18.0)	16.2 (23.3)	15.9 (20.6)
Median (range)	13 (0, 50)	0 (0, 75)	0 (0, 75)
Missing	2	4	6
N	16	17	33
The decision was a wise one			
Mean (s.d.)	19.1 (18.8)	16.3 (29.6)	17.6 (24.9)
Median (range)	25 (0, 50)	0 (0, 100)	0 (0, 100)
Missing	1	1	2
N	17	20	37

Decision regret regarding decision to accept the randomised treatment

	Radical Cystectomy	BCG immunotherapy	Total
It was the right decision			
Mean (s.d.)	11.8 (12.9)	18.1 (24.0)	15.0 (19.4)
Median (range)	0 (0, 25)	0 (0, 75)	0 (0, 75)
Missing	1	3	4
N	17	18	35
I regret the choice that was made			
Mean (s.d.)	13.2 (15.6)	22.1 (27.8)	17.6 (22.6)
Median (range)	0 (0, 50)	0 (0, 75)	0 (0, 75)
Missing	1	4	5
N	17	17	34
I would go for the same choice if I had to do it over again			
Mean (s.d.)	13.2 (15.6)	16.7 (24.3)	15.0 (20.3)
Median (range)	0 (0, 50)	0 (0, 75)	0 (0, 75)
Missing	1	3	4
N	17	18	35
The choice did me a lot of harm			
Mean (s.d.)	17.6 (14.7)	20.6 (26.9)	19.1 (21.4)
Median (range)	25 (0, 50)	0 (0, 75)	25 (0, 75)
Missing	1	4	5
N	17	17	34
The decision was a wise one			
Mean (s.d.)	14.7 (17.8)	19.4 (25.1)	17.1 (21.7)
Median (range)	0 (0, 50)	0 (0, 75)	0 (0, 75)
Missing	1	3	4
N	17	18	35

All scores have been converted to a 0-100 scale in which a higher value indicates more regret. 'I regret the choice that was made' and 'The choice did me a lot of harm' have been reverse coded such that a higher value also indicates more regret. A final score has been calculated, which is simply the mean of all scores.