1 Supplementary Table 1. A checklist for the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3, 4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	-
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5, Figure 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	-
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	-
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6, 9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6, 7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6, Supplementary Tables 2-8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Supplementary Tables 2-8
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	-
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	6
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11, 12
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	13-15

Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	13, 14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14,15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	15,16

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

9 Supplementary Table 2. Summary associations for previously reported SNPs on age at the time of diagnosis for urinary bladder cancer.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
An increase in age at the time of diagnosis:															
>56 years	2009	Stern et al. [1]	Low-risk NMIBC (Ta+G1/G2)	UC	Caucasian (Northern American)	297 (>55 years) / 201 (≤55 years)	rs710521	3q28	TP63	A	G	0.80 (1KG)	OR (A/G)=1.77	1.22-2.56	<0.05
≥65 years / Age of healthy controls	2010	Yuan et al. [2]	UBC	UC	Chinese	214 (UBC cases) / 212 (Healthy controls)	G870A (rs9344)	11q13.3	CCND1	A	G	0.41 (1KG)	OR (AG+AA/GG)=1.74	1.06-2.88	0.029
>65 years	2012	Ma et al. [3]	UBC	UC	Chinese	450 (GG) / 808 (CG+CC)	rs1052133	3p25.3	OGG1	G	C	0.30 (1KG)	OR (GG/CG+CC)=1.31	1.04-1.66	p<0.05
>65 years	2013	Chu et al. [4]	UBC	UC	Chinese	475 (CC) / 632 (CT+TT)	3'UTR 774T>C (rs884225)	7p11.2	EGFR	C	T	0.19 (1KG)	OR (CC/CT+TT)=1.87	1.39–2.53	<0.05
>65 years	2008	Wang et al. [5]	UBC	UC	Chinese	103 (Age >65 years) / 113 (Healthy controls)	6721G>T (rs7003908)	8q11.21	XRCC7 (PRKDC)	T	G	0.33 (1KG)	OR (TT/GT+GG)=2.27	1.25-4.10	0.007
>60 years	2018	Wang et al. [6]	UBC	Not reported	Chinese	690 (AG+AA) / 1015 (GG)	rs874945	12q13.13	HOTAIR	A	G	0.36 (1KG)	OR (AA+AG/GG)=1.35	1.10-1.65	0.004
A decrease in age at the time of diagnosis:															
≤60 years	2016	Hua et al. [7]	UBC	UC	Chinese	60 (AA) / 296 (GG+GA)	rs217727	11p15.5	H19 (lncRNA)	A	G	0.36 / 0.20 (1KG)	OR (AA / GG+GA)=1.80	1.16–2.81	0.009
≤65 years / Healthy controls	2009	Wang et al. [8]	UBC	UC	Chinese	203 (≤65 years) / 238 (Healthy controls)	rs9642880	8q24.21	CASC11	T	G	0.54 (1KG)	OR (GT+TT/GG)=2.31	1.56–3.43	<0.0001
≥50 years	2004	Kelsey et al. [9]	UBC	UC + Other	Caucasian (Northern American)	29 (AA) / 294 (AG+GG)	Codon 399 (rs25487)	19q13.2	XRCC1	A	G	0.26 (1KG)	OR (AA / AG+GG)=0.6	0.3-0.9	<0.05
Age, years	2010	Kiemeney et al. [10]	UBC	UC	European (Multiple)	4211	rs798766	4p16.3	TACC3/FGFR3	T	C	0.23 / 0.24 (1KG)	β=-0.81	-1.35; -0.26	0.0036

>65 years	2015	Xiao et al. [11]	UBC	Not reported	Chinese	548 (UBC) / 709 (Healthy controls)	rs1057868	7q11.23	POR	T	C	0.29 (1KG)	OR (TT/CT+CC)=0.586	0.417-0.823	0.002
>60 years	2017	Lin et al. [12]	UBC	UC	Chinese	673 (AG+GG) / 1015 (AA)	rs710886	8q24.21	PCAT1	G	A	0.47 (1KG)	OR (AG+GG/AA)=0.77	0.67-0.88	<0.001

CI-confidence interval; EA-effect allele; EAF-effect allele frequency; NMIBC-non-muscle-invasive bladder cancer; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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Supplementary Table 3. Summary associations for previously reported SNPs on urinary bladder cancer tumor size at the time of diagnosis.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
Associations for an increase in tumor size:															
Tumor size (≥3 cm)	2014	Gu et al. [1]	UBC	Not reported	Chinese	218 (G3) / 670 (Healthy subjects)	696 C/T (rs2664139)	15q14	TSP-1 (THBS1)	C	T	0.43 (1KG)	OR (CC/TT+CT)=1.94	1.22-3.10	0.006
Associations for a decrease in tumor size:															
Tumor size (T1-T4)	2018	Lee et al. [2]	UBC	UC	Taiwanese	279 (T1-T4) / 90 (Ta)	rs2929973	8q24.22	WISP1 (CCN4)	G	T	0.17 (1KG)	OR (TG+GG/TT)=0.61	0.371-0.990	0.044

CI-confidence interval; EA-effect allele; EAF-effect allele frequency; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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60 Supplementary Table 4. Summary associations for previously reported SNPs on stage at the time of diagnosis for urinary bladder cancer.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
Associations for stages of Ta/T1/Tis (or combinations of these):															
Associations reducing the risk of stages of Ta/T1/Tis (or combinations of these):															
Ta+T1	2004	Kelsey et al. [1]	UBC	UC + Other	Caucasian (Northern American)	22 (AA) / 234 (AG+GG)	Codon 399 (rs25487)	19q13.2	XRCC1	A	G	0.26 (1KG)	OR (AA / AG+GG)=0.5	0.3-0.9	<0.05
Ta+T1	2011	Safarinejad et al. [2]	UBC (men only)	UC	Iranian	102 (Ta+T1)	rs2274976	1p36.22	MTHFR	A	G	0.07 (1KG)	OR (A/G)=0.57	0.41-0.75	0.012
Ta+T1	2011	Safarinejad et al. [2]	UBC (men only)	UC	Iranian	102 (Ta+T1)	rs1801133	1p36.22	MTHFR	T	C	0.25 (1KG)	OR (T/C)=0.47	0.36–0.68	0.001
Ta+T1	2011	Safarinejad et al. [2]	UBC (men only)	UC	Iranian	102 (Ta+T1)	rs1801131	1p36.22	MTHFR	C	A	0.25 (1KG)	OR (C/A)=0.46	0.28-0.71	0.001
Ta+T1	2011	Sobti et al. [3]	UBC	Not reported	Indian	18 (CC) / 127 (GG)	RAD51 135 G/C (rs1801320)	15q15.1	RAD51	C	G	0.26 (Cases) / 0.31 (Controls) / 0.14 (1KG)	OR (CC/GG)= 0.51	0.27–0.99	0.031
Ta+T1+Tis / Healthy controls	2008	Verhaegh et al. [4]	NMIBC	Not reported	European (The Netherlands)	83 (NMIBC) / 152 (Healthy controls)	rs2839698	11p15.5	H19	C	T	0.71 (1KG)	OR (TC/TT)=0.52	0.28-0.94	<0.05
Ta+T1+Tis / Healthy controls	2015	Zhao et al. [5]	UBC	Not reported	Chinese	76 (Tis+Ta+T1) / 210 (Healthy controls)	429 CT genotype (rs2227485)	12q15	IL22	T	C	0.48 (all UBC) / 0.49 (1KG)	OR (TT / CT+CC)=0.48	0.23-0.9	0.04

Ta+T1	2018	Ahmed et al. [6]	NMIBC	UC	Pakistani	248 (NMIBC) / 400 (Controls) (Allele count instead of individuals)	rs861539	14q32.33	XRCC3	T	C	0.22 (1KG)	OR (T/C)=0.63	0.43-0.94	<0.05
Associations increasing the risk for stages of Ta/T1/Tis (or combinations of these):															
Ta+T1	2010	Yuan et al. [7]	UBC	UC	Chinese	255 (Ta+T1 / 402 (Healthy controls)	G870A (rs9344)	11q13.3	CCND1	A	G	0.41 (1KG)	OR (AG+AA/GG)=1.86	1.10-3.16	0.021
Ta+T1 / Healthy controls	2002	Chen et al. [8]	UBC	UC	Taiwanese	33 (Ta+T1) / 119 (Healthy controls)	Ser31Arg (rs1801270)	6p21.2	P21 (CDKN1A)	A	C	0.74 (Cases) / 0.57 (Controls) / 0.26 (1KG)	OR (A/C)=2.55	1.54-4.79	0.012
Ta+T1 / Healthy controls	2008	Gangwar et al. [9]	NMIBC	UC	Indian	76 (Ta+T1) / 146 (Healthy controls)	Asp312Asn (G>A) (rs1799793)	19q13.3	ERCC2	A	G	0.19 (1KG)	OR(AA/GG)=4.62	2.29-9.29	0.003
Ta+T1 / Healthy controls	2009	Wen et al. [10]	NMIBC	Not reported	Chinese	304 (Cases) / 90 (Healthy controls)	Lys939Gln (rs2228001)	3p25.1	XPC	C	A	0.32 (1KG)	OR (AC+CC/AA)=1.89	1.21-3.24	0.02
Ta+T1 / T2+	2004	Ichimura et al. [11]	UBC	UC	Japanese	152 (Ta+T1) / 42 (T2+)	Pro198Leu (rs1050450)	3p21.31	GPX1	T	C	0.22 (1KG)	OR (CT/CC)=2.58	1.07-6.18	0.034
Ta+T1+Tis / Healthy controls	2017	Ali et al. [12]	UBC	UC	Pakistani	124 (Ta+T1) / 200 (Healthy controls)	rs1137101	1p31.3	LEPR	A	G	0.52 (Cases) / 0.42 (Controls) / 0.42 (1KG)	OR (G/A)=1.4	1.04–2	<0.05
Tis (or multiple tumors)	2011	Lima et al. [13]	NMIBC	Not reported	European (Portugal)	65 (Multiple/CIS) / 52 (Single)	IL4-590C/T (rs2243250)	5q31.1	IL4	T	C	0.47 (1KG)	OR (T/C) =2.80	1.08-7.27	0.031

Tis / Ta+T1	2004	Ito et al. [14]	NMIBC	UC	Japanese	14 (Tis)/ 47 (no Tis)	G870A (rs9344)	11q13.3	CCND1	A	G	0.41 (1KG)	OR (AG/GG)=3.67 OR (AA/AG+GG)=3.94	1.00-13.45 1.40-11.10	0.049 0.009
T1	2013	Pandith et al. [15]	UBC	UC	Indian	18 (TC+CC) / 32 (TT)	rs12628	11p15.5	HRAS	C	T	0.30 (1KG)	OR (TC+CC/TT)=3.0	1.50–5.97	0.004
Ta+T1 (patients ≤71 yrs)	2006	Sakano et al. [16]	NMIBC	UC	European (Sweden)	30 (T1) / 83 (Ta)	Asp1104His (rs17655)	13q33.1	XPG (ERCC5)	C	G	0.36 (1KG)	OR (GC+CC/GG)=4.9	2.0-12.9	<0.001
Ta+T1	2018	Ahmed et al. [6]	NMIBC	UC	Pakistani	65 (NMIBC) / 99 (Controls)	rs2304277	3p25.3	OGG1	G	A	0.65 (1KG)	OR (GG/AA)=4.03	1.87–8.67	<0.05
Ta+T1	2018	Ahmed et al. [6]	NMIBC	UC	Pakistani	248 (NMIBC) / 400 (Controls) (Allele count instead of individuals)	rs2304277	3p25.3	OGG1	G	A	0.65 (1KG)	OR (G/A)=1.78	1.25-2.53	<0.05
Ta+T1	2018	Ahmed et al. [6]	NMIBC	UC	Pakistani	107 (NMIBC) / 184 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (AC/AA)=2.14	1.20–3.81	<0.05
Ta+T1	2018	Ahmed et al. [6]	NMIBC	UC	Pakistani	92 (NMIBC) / 167 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (CC/AA)=2.52	1.17-5.41	<0.05
Ta+T1	2018	Ahmed et al. [6]	NMIBC	UC	Pakistani	248 (NMIBC) / 400 (Controls) (Allele count instead of individuals)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (C/A)=1.72	1.21-2.43	<0.05
Ta+T1	2018	Ahmed et al. [6]	NMIBC	UC	Pakistani	248 (NMIBC) / 400 (Controls) (Allele count instead of individuals)	rs1052133	3p25.3	OGG1	G	C	0.30 (1KG)	OR (G/C)=1.57	1.03-2.37	<0.05
Associations for stages of T2+:															
Associations reducing the risk of stages of T2+:															

T2+	2009	Ahirwar et al. [17]	UBC	UC	Indian	82 (T2+) / 132 (Ta+T1)	857C>T (rs1799724)	6p21.33	TNFA	T	C	0.09 (1KG)	OR (CT/CC)=0.52	0.27-0.99	0.049
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs6463524 (merged into rs1805319)	7p22.1	PMS2	G?	A/C/T?	G=0.17 (1KG)	OR (G?/A?C?T?)=0.56	0.41-0.77	0.0002
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs3213427	12p13.31	CD4	C?	T?	C=0.26 (1KG)	OR (C?/T?)=0.71	0.57-0.88	0.001
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs828702	2q35	XRCC5	G?	A?	G=0.45 (1KG)	OR (G?/A?)=0.80	0.65-0.99	0.037
T2+	2010	Gangwar et al. [19]	UBC	UC	Indian	34 (T2+) / 25 (TaG1)	T309G (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	OR (GG/TT)=0.30	0.09-0.99	0.049
T2+ / Ta+T1	2015	Deng et al. [20]	UBC	Not reported	Chinese	84 (Invasive) / (75 (Superficial)	rs2910164	5q33.3	MIR146A	G	C	0.39 (all UBC) / 0.32 (TOPMED)	OR (GG / CG+CC)=0.20	0.05–0.72	0.012
T2+ / Ta+T1	2011	Safarinejad et al. [21]	UBC	UC	Iranian	56 (T2+) / 84 (Ta+T1) 37 (T2+) / 40 (Ta+T1)	rs2854744	7p12.3	IGFBP3	A	C	0.39 (UBC) / 0.49 (Healthy controls) / 0.47 (1KG)	OR (AC/CC)=0.32 OR (AA/CC)= 0.17	0.24–0.52 0.11–0.31	0.0001 0.00001
T2+ / Ta+T1	2011	Lin et al. [22]	UBC	UC	Taiwanese	34 (T2+) / 58 (Ta+T1)	CCND1 G870A (rs9344)	11q13.3	CCND1	G	A	0.59 (1KG)	OR (AG/AA)=0.29	0.12-0.70	0.009
T2+ / Ta+T1	2013	Safarinejad et al. [23]	UBC	UC	Iranian	59 (T2+) / 107 (Ta+T1)	rs1695	11q13.2	GSTP1	G	A	0.35 (1KG)	OR (AG+GG/AA)= 0.72	0.51-0.87	0.002
T2+ / TaG1	2009	Gangwar et al. [24]	UBC	UC	Indian	59 (T2+) / 34 (TaG1)	1263A>G (rs 4645978)	1p36.21	CASP9	G	A	0.42 (1KG)	OR (AG/AA)=0.28	0.10-0.76	0.013

T2+ / TaG1	2013	Jaiswal et al. [25]	UBC	UC	Indian	50 (MIBC) / 36 (NMIBC)	IL18(−137) G/C (rs187238)	11q23.1	IL18	C	G	0.79 (1KG)	OR (GC/GG)=0.36	0.15–0.89	0.027
T2+ / Healthy controls	2017	Ali et al. [12]	UBC	UC	Pakistani	76 (T2+) / 200 (Healthy controls)	rs1801282	3p25.2	PPARG	G	C	0.16 (Cases) / 0.12 (Controls) / 0.07 (1KG)	OR (GG/CC)=5.4	1.2–24	<0.05
Associations increasing the risk for stages of T2+:															
T1+T2+ / Ta	2007	Sanyal et al. [26]	UBC	Not reported	European (Sweden)	106 (T1+T2+) / 146 (Ta)	G39E (rs1042821)	2p16.3	MSH6	A	G	0.20 (1KG)	RR (AG+AA/GG)=1.9	1.1-3.2	0.03
T1+T2+ / Ta	2007	Sanyal et al. [27]	UBC	Not reported	European (Sweden)	103 (T1+T2+) / 145 (Ta)	P187S (rs1800566)	16q22.1	NQO1	T	C	0.29 (1KG)	RR (CT+TT/CC)=1.8	1.0-3.1	0.04
T2+	2007	Sanyal et al. [27]	UBC	Not reported	European (Sweden)	40 (AG+GG) / 25 (AA)	I105V (rs1695)	11q13.2	GSTP1	G	A	0.35 (1KG)	RR (AG+GG/AA)=2.7	1.3-5.6	0.008
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs11738738	5q31.2	MATR3	A?	C/T	A=0.39 (1KG)	OR (A?/C?T?)=1.26	1.02-1.56	0.032
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs2274700	1q31.3	CFH	A?	C/G/T?	A=0.48 (1KG)	OR (A?/C?G?T?)=1.24	1.00-1.52	0.046
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs6596471	5q31.2	SLC23A1	A?	C/G/T?	A=0.48 (1KG)	OR (A?/C?G?T?)=1.29	1.05-1.60	0.019
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs10063949	5q31.2	SLC23A1	T?	C?	T=0.42 (1KG)	OR (T?/C?)=1.25	1.01-1.54	0.039
T2+	2009	Guey et al. [18]	UBC	UC	European (Spain)	246 (Only reported overall)	rs4315920	5q31.2	DNAJC18	A?	G?	A=0.46 (1KG)	OR (A?/G?)=1.31	1.06-1.62	0.013
T2+	2010	Wang et al. [28]	UBC	UC	Chinese	115 (CT/TT) / 86 (CC)	rs2294008	8q24.3	PSCA	T	C	0.60 (1KG)	OR (CT+TT/CC)=1.65	1.18-2.31	0.003
T2+	2010	Safarinejad et al. [2]	UBC (men only)	UC	Iranian	56 (T2+)	rs2274976	1p36.22	MTHFR	A	G	0.07 (1KG)	OR (A/G)=3.55	2.42–5.71	0.001
T2+	2010	Safarinejad et al. [2]	UBC (men only)	UC	Iranian	56 (T2+)	rs1801133	1p36.22	MTHFR	T	C	0.25 (1KG)	OR (T/C)=3.52	2.25–5.37	0.001
T2+	2010	Safarinejad et al. [2]	UBC (men only)	UC	Iranian	56 (T2+)	rs1801131	1p36.22	MTHFR	C	A	0.25 (1KG)	OR (C/A)=3.62	2.35–5.67	0.001
T2+	2013	Pandith et al. [15]	UBC	UC	Indian	25 (TC+CC) / 40 (TT)	rs12628	11p15.5	HRAS	C	T	0.30 (1KG)	OR (TC+CC/TT)=3.3	1.71–6.30	<0.001

T2+	2012	Zhou et al. [29]	UBC	UC	Chinese	115 (AG+AA) / 29 (GG)	rs2275913	6p12.2	IL17	A	G	0.29 (1KG)	OR (AG+AA/GG)= 1.79	1.04-3.03	0.032
T2+	2013	Chu et al. [30]	MIBC	UC	Chinese	81 (CC) / 238 (CT+TT)	3'UTR 774T>C (rs884225)	7p11.2	EGFR	C	T	0.19 (1KG)	OR (CC/CT+TT)=1.40	1.05–1.89	<0.05
T2+	2016	Hua et al. [31]	UBC	UC	Chinese	56 (AA) / 3015 (GG+GA)	rs217727	11p15.5	H19 (lncRNA)	A	G	0.36 / 0.20 (1KG)	OR (AA/GG+GA)=1.48	1.06–2.06	0.022
T2+ / Healthy controls	2002	Chen et al. [8]	UBC	UC	Taiwanese	20 (T2+) / 119 (Healthy controls)	Ser31Arg (rs1801270)	6p21.2	P21 (CDKN1A)	A	C	0.74 (Cases) / 0.57 (Controls) / 0.26 (1KG)	OR (A/C)= 1.55	0.77-3.12	0.01
T2+ / Healthy controls	2009	Gangwar et al. [32]	UBC	UC	Indian	43 (T2+) / 134 (Healthy controls)	rs7003908	8q11.21	XRCC7 (PRKDC)	G	T	0.33 (1KG)	OR (GG/TT)=6.80	2.30-15.75	<0.001
T2+ / Healthy controls	2012	Lin et al. [33]	MIBC	Not reported	Taiwanese	42 (CC) / 151 (CT+TT)	p53 codon 72 (rs1042522)	17p13.1	TP53	C	G	0.63 (Cases) / 0.67 (Controls) / 0.54 (1KG)	OR (CC/CT+TT)=3.36	1.58–7.15	0.002
T2+ / Ta+T1	2005	Leibovici et al. [34]	UBC	Not reported	Caucasian (White)	203 (T2+) / 238 (Ta+T1)	rs1800629	6p21.33	TNFA	A	G	0.09 (1KG)	OR (AG+AA/GG)=1.91	1.27-2.89	<0.05
T2+ / Ta+T1	2005	Leibovici et al. [34]	UBC	Not reported	Caucasian (White)	187 (T2+) / 232 (Ta+T1)	Pro12Ala (rs1801282)	3p25.2	PPARG	G	C	0.07 (1KG)	OR (CG+GG/CC)=1.61	1.03-2.53	<0.05
T2+ / Ta+T1	2007	Kader et al. [35]	UBC	Not reported	Caucasian (Northern American)	241 (MIBC) / 314 (NMIBC)	A82G (rs2276109)	11q22.2	MMP12	G	A	0.06 (1KG)	OR (AG+GG/AA)=1.50	1.00-2.28	<0.05
T2+ / Ta+T1	2012	Kucukgergin et al. [36]	UBC	UC	Turkish	20 (T2+) / 71 (Ta+T1)	Pro198Leu (rs1050450)	3p21.31	GPX1	T	C	0.22 (1KG)	OR (TT/CC)=4.13	1.98–8.58	<0.001
T2+ / Ta+T1	2012	Guirado et al. [37]	UBC	UC	European (Spain)	92 (T2+) / 136 (Ta+T1)	rs3764147	13q14.11	C13ORF31 (LACC1)	T	C	0.7 (1KG)	OR (TT/CT)=1.87	1.05–3.32	0.033

T2+ / Ta+T1	2012	Guirado et al. [37]	UBC	UC	European (Spain)	98 (T2+) / 148 (Ta+T1)	rs4129009	4p14	TLR10	T	C	0.85 (1KG)	OR (TT/CT+CC)=1.75	1.04-2.94	0.033
T2+ / Ta+T1	2012	Kucukgergin et al. [38]	UBC	UC	Turkish	27 (T2+) / 105 (Ta+T1)	rs2228014	2q2	CXCR4	T	C	0.06 (1KG	OR (CT+TT/CC)=1.61	1.03-2.52	0.035
T2+ / Ta+T1	2012	Kucukgergin et al. [38]	UBC	UC	Turkish	20 (T2+) / 85 (Ta+T1) 27 (T2+) / 115 (Ta+T1)	CCR2 V64I (rs1799864)	3p21.31	CCR2	A	G	0.15 (1KG)	OR (AA/GG)=6.56 OR (AG+AA/GG)=1.66	2.18–19.7 1.06–2.60	0.001 0.026
T2+ / Ta+T1	2012	Kucukgergin et al. [38]	UBC	UC	Turkish	20 (T2+) / 64 (Ta+T1)	rs1801157	10q11.21	SDF1 (CXCL12)	A	G	0.19 (1KG)	OR (AA/GG)=1.93	1.11–3.38	0.02
T2+ / Ta+T1	2013	Wen et al. [39]	UBC	UC	Chinese	36 (MIBC) / 94 (NMIBC)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	Chi-square = 18.89	N/A	<0.001
T2+ / Ta+T1	2014	Zhang et al. [40]	UBC	UC	Chinese	151 (MIBC) / 174 (NMIBC)	rs61330082	7q22.3	NAMPT	C	T	0.73 (1KG)	OR (CT/CC+TT)=1.70	1.01–2.87	<0.05
T2+ / Ta+T1	2014	Zhou et al. [41]	UBC (excluding Tis)	UC	Chinese	156 (T2+) / 176 (Ta+T1)	rs3756712	5p15.33	PDCD6	G	T	0.40 (1KG)	OR (GG/GT+TT)=3.33	1.23–10.00	<0.05
T2+ / Ta+T1	2015	Weng et al. [42]	UBC	UC	Taiwanese	108 (T2+) / 167 (Ta+T1)	rs187115	11p13	CD44	G	A	0.20 (all UBC) / 0.35 (1KG)	OR (AA/AG+GG)=1.69	1.020–2.793	0.041
T2+ / TaG1	2008	Mittal et al. [43]	NMIBC	UC	Indian	32 (T2+) / 25 (TaG1)	Codon 194 (rs1799782)	19q13.2	XRCC1	T	C	0.12 (1KG)	OR (CT+TT/CC)=11.00	1.29-92.30	0.03
T2+ / TaG1	2010	Gangwar et al. [44]	UBC	UC	Indian	63 (T2+) / 35 (TaG1)	Lys939Gln (rs2228001)	3p25.1	XPC	C	A	0.32 (1KG)	OR (AC+CC/AA)=2.52	1.03-6.14	0.041
T2+ / TaG1	2011	Gangwar et al. [45]	MIBC	UC	Indian	63 (T2+) / 33 (TaG1)	rs20417	1q31.1	COX2 (PTGS2)	C	G	0.80 (1KG)	OR (GC/GG)=2.73	1.08-6.88	0.033
T2+/Ta, T1	2015	Zhou et al. [46]	UBC	UC	Chinese	156 (MIBC) / 176 (NMIBC)	rs17855750	16p12.1-p11.2	IL27	G	T	0.07 (1KG)	OR (TG+GG/TT)=2.04	1.02–4.17	0.042
T2+ / Ta+T1	2010	Pandith et al. [47]	UBC	UC + Other	Indian	59 (T2+) / 49 (T1+T1)	Arg72Pro (rs1042522)	17p13.1	TP53	C	G	0.54 (1KG)	OR (CC+CG/GG)=4.2	1.5-11.3	0.004
T2+ / Ta+G1	2012	Mittal et al. [48]	UBC	Not reported	Indian	29 (T2+) / 16 (Ta+G1)	Exon 10 (rs1799793)	19q13.32	XPD (ERCC2)	A	G	0.19 (1KG)	OR (AA/GG)=4.53	1.05-19.4	0.042

T2+	2018	Ahmed et al. [6]	MIBC	UC	Pakistani	50 (MIBC) / 99 (Controls)	rs2304277	3p25.3	OGG1	G	A	0.65 (1KG)	OR (GG/AA)=3.06	1.31–7.13	<0.05
T2+	2018	Ahmed et al. [6]	MIBC	UC	Pakistani	65 (MIBC) / 184 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (AC/AA)=2.95	1.51–5.75	<0.05
T2+	2018	Ahmed et al. [6]	MIBC	UC	Pakistani	52 (MIBC) / 167 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (CC/AA)=3.18	1.32-7.66	<0.05
T2+	2018	Ahmed et al. [6]	MIBC	UC	Pakistani	152 (MIBC) / 400 (Controls) (Allele count instead of individuals)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (C/A)=2.02	1.36-3.01	<0.05
T2+	2018	Ahmed et al. [6]	MIBC	UC	Pakistani	57 (MIBC) / 136 (Controls)	rs1052133	3p25.3	OGG1	G	C	0.30 (1KG)	OR (GG/CC)=5.95	1.37-25.7	<0.05

CI-confidence interval; EA-effect allele; EAF-effect allele frequency; MIBC-muscle-invasive bladder cancer; NMIBC-non-muscle-invasive bladder cancer; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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172 Supplementary Table 5. Summary associations for previously reported SNPs on tumor grade at the time of diagnosis for urinary bladder
173 cancer.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
Associations for G1 and G2 (or combinations of these):															
Associations reducing the risk of G1 and G2 (or combinations of these):															
G1+G2	2011	Safarinejad et al. [1]	UBC (men only)	UC	Iranian	115 (G1+G2)	rs1801133	1p36.22	MTHFR	T	C	0.25 (1KG)	OR (T/C)=0.46	0.35–0.66	0.001
G1+G2	2011	Safarinejad et al. [1]	UBC (men only)	UC	Iranian	115 (G1+G2)	rs1801131	1p36.22	MTHFR	C	A	0.25 (1KG)	OR (C/A)=0.45	0.26-0.70	0.001
G2	2011	Sobti et al. [2]	UBC	Not reported	Indian	6 (CC) / 92 (GG)	RAD51 135 G/C (rs1801320)	15q15.1	RAD51	C	G	0.26 (Cases) / 0.31 (Controls) / 0.14 (1KG)	OR (CC/GG)= 0.24	0.09–0.62	0.0008
Low grade UBC	2015	Xie et al. [3]	UBC	UC	Chinese	211 (Low grade) / 649 (Controls)	SNP309 T>G (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	OR (TG+GG/TT)=0.613	0.427-0.881	0.008
Associations increasing the risk of G1 and G2 (or combinations of these):															
G1	2010	Yuan et al. [4]	UBC	UC	Chinese	164 (G1) / 402 (Healthy controls)	G870A (rs9344)	11q13.3	CCND1	A	G	0.41 (1KG)	OR (AG+AA/GG)=1.81	1.10-2.97	0.019
G1	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	827 (G1) / 5,117 (Healthy controls)	rs798766	4p16.3	TMEM129 TACC3-FGFR3	T	C	0.24 (1KG)	OR (T/C)=1.27	1.11-1.44	3.00E-04
G1	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	826 (G1) / 5,117 (Healthy controls)	rs401681	5p15.33	CLPTM1L	C	T	0.59 (1KG)	OR (C/T)=1.22	1.09-1.36	3.20E-04

G1	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	825 (G1) / 5,108 (Healthy controls)	rs9642880	8q24.21	MYC	T	G	0.54 (1KG)	OR (T/G)=1.20	1.08-1.34	7.50E-04
G1 / G2+Ta	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	1,147 (G2) / 2,539 (Healthy controls)	rs798766	4p16.3	TMEM129 TACC3-FGFR3	T	C	0.24 (1KG)	OR (T/C)=1.28	1.14-1.45	4.80E-05
G1 / G2+Ta	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	1,145 (Low-risk) / 2,532 (Healthy controls)	rs9642880	8q24.21	MYC	T	G	0.54 (1KG)	OR (T/G)=1.25	1.13-1.38	8.60E-06
G1 / Healthy controls	2008	Gangwar et al. [6]	UBC	UC	Indian	64 (G1) / 232 (Healthy controls) 36 (G1) / 146 (Healthy controls)	Asp312Asn (G>A) (rs1799793)	19q13.3	ERCC2	A	G	0.19 (1KG)	OR (AG/GG)=2.51 OR (AA/GG)=5.21	1.39-4.54 2.23-12.1	0.006 0.003
G1+G2	2011	Safarinejad et al. [1]	UBC (men only)	UC	Iranian	115 (G1+G2)	rs2274976	1p36.22	MTHFR	A	G	0.07 (1KG)	OR (G/A)=3.32	2.25-5.46	0.001
G2	2010	Wang et al. [7]	UBC	UC	Chinese	123 (Invasive) / 106 (Superficial)	rs2294008	8q24.3	PSCA	T	C	0.60 (1KG)	OR (CT+TT/CC)=1.43	1.05-1.96	0.024
G2	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	856 (G2) / 5,117 (Healthy controls)	rs798766	4p16.3	TMEM129 TACC3-FGFR3	T	C	0.24 (1KG)	OR (T/C)=1.21	1.07-1.37	2.80E-03
G2	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	825 (G2) / 5,108 (Healthy controls)	rs9642880	8q24.21	MYC	T	G	0.54 (1KG)	OR (T/G)=1.22	1.10-1.36	2.10E-04
G2 / Healthy controls	2008	Gangwar et al. [6]	UBC	UC	Indian	45 (G2) / 146 (Healthy controls)	Asp312Asn (G>A) (rs1799793)	19q13.3	ERCC2	A	G	0.19 (1KG)	OR (AA/GG)=4.67	1.72-12.6	0.002
G1+G2+papilloma / Healthy controls	2017	Ali et al. [8]	UBC	UC	Pakistani	133 (G2+G1) / 200 (Healthy controls)	rs1137101	1p31.3	LEPR	A	G	0.52 (Cases) / 0.42 (Controls) / 0.42 (1KG)	OR (G/A)=1.4	1.1–2	<0.05
G1	2018	Ahmed et al. [9]	UBC	UC	Pakistani	61 (Low grade UBC) / 99 (Controls)	rs2304277	3p25.3	OGG1	G	A	0.65 (1KG)	OR (GG/AA) = 3.73	1.72–8.09	<0.05

G1	2018	Ahmed et al. [9]	UBC	UC	Pakistani	234 (Low grade UBC) / 400 (Controls) (Allele count instead of individuals)	rs2304277	3p25.3	OGG1	G	A	0.65 (1KG)	OR (G/A)=1.72	1.20-2.46	<0.05
G1	2018	Ahmed et al. [9]	UBC	UC	Pakistani	100 (Low grade UBC) / 184 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (AC/AA)=2.18	1.21–3.92	<0.05
G1	2018	Ahmed et al. [9]	UBC	UC	Pakistani	87 (Low grade UBC) / 167 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (CC/AA)=2.55	1.20-5.44	<0.05
G1	2018	Ahmed et al. [9]	UBC	UC	Pakistani	234 (Low grade UBC) / 400 (Controls) (allele count instead of individuals)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (C/A)=1.72	1.22-2.44	<0.05
Low grade UBC	2018	Li et al. [10]	UBC	Not reported	Chinese	127 (Low grade UBC) / 167 (High grade UBC)	rs4758680	12q24.31	IL31	A	C	0.29 (1KG)	OR (CA+AA/CC)=2.34	1.25-4.40	0.007
Associations for G3 (or other definitions of High grade):															
Associations reducing the risk of G3 (or High grade):															
G3	2011	Safarinejad et al. [1]	UBC (men only)	UC	Iranian	43 (G3)	rs2274976	1p36.22	MTHFR	A	G	0.07 (1KG)	OR (G/A)=0.55	0.44–0.72	0.014
G3 / G2, G1? (Not explicitly stated)	2016	Wu et al. [11]	UBC	Not reported	Chinese	180 (G3) / 153 (G2+G1)	rs353293	5q32	MIR143 (microRNA 143) / CARMN	A	G	10.1 (all UBC cases) / 0.26 (1KG)	OR (A/G)=0.54	0.32–0.92	0.02
G3 / G1+G2	2011	Safarinejad et al. [12]	UBC	UC	Iranian	46 (G3) / 94 (G1+G2) 31 (G3) / 44 (G1+G2)	rs2854744	7p12.3	IGFBP3	A	C	0.39 (UBC) / 0.49 (Healthy controls) / 0.47 (1KG)	OR (AC/CC)= 0.34 OR (AA/CC)= 0.21	0.24–0.68 0.12–0.42	0.0001 0.00001

G3 / G1+G2	2013	Safarinejad et al. [13]	UBC	UC	Iranian	47 (G3) / 119 (G1+G2))	rs1695	11q13.2	GSTP1	G	A	0.35 (1KG)	OR (AG+GG/AA)= 0.62	0.48-0.79	0.002
G3 / Healthy controls	2017	Ali et al. [8]	UBC	UC	Pakistani	67 (High grade) / 200 (Healthy controls)	rs2854744	7p12.3	IGFBP3	A	C	0.44 (Cases) / 0.51 (Controls) / 0.53 (1KG)	OR (CA/CC)=0.5	0.3–0.98	<0.05
High grade (G2B+G3) NMIBC / Low grade (G1+G2A) NMIBC (>71 year-old group)	2006	Sakano et al. [14]	NMIBC	UC	European (Sweden)	48 (High grade) / 64 (Low-group)	Asp1104His (rs17655)	13q33.1	XPG (ERCC5)	C	G	0.36 (1KG)	OR (GC+CC/GG)=0.3	0.1-0.7	0.004
Associations increasing the risk of G3 (or High grade):															
G3	2010	Rothman et al. [5]	UBC	Not reported	Multi-ethnic	1.338 (G3) / 6,170 (Healthy controls)	rs8102137	19q12	CCNE1	C	T	0.16 (1KG)	OR (C/T)=1.23	1.13-1.35	4.60E-06
G3	2011	Safarinejad et al. [1]	UBC (men only)	UC	Iranian	43 (G3)	rs1801133	1p36.22	MTHFR	T	C	0.25 (1KG)	OR (T/C)=3.55	2.32–5.41	0.001
G3	2011	Safarinejad et al. [1]	UBC (men only)	UC	Iranian	43 (G3)	rs1801131	1p36.22	MTHFR	C	A	0.25 (1KG)	OR (C/A)=3.67	2.37–5.71	0.001
G3	2013	Pandith et al. [15]	UBC	UC	Indian	31 (TC+CC) / 31 (TT)	rs12628	11p15.5	HRAS	C	T	0.30 (1KG)	OR (TC+CC/TT)=5.4	2.8–10.2	<0.001
G3	2016	Hua et al. [16]	UBC	UC	Chinese	31 (AA) / 132 (GG+GA)	rs217727	11p15.5	H19 (lncRNA)	A	G	0.36 / 0.20 (1KG)	OR (AA / GG+GA)=1.89	1.23–2.91	0.004
G3 / G1+G2	2015	Timirci-Kahraman et al. [17]	UBC	UC	Turkish	28 (G3) / 52 (G1+G2)	rs4871857 (has merged into rs20575)	8p21.3	DR4 (TNFRSF10A)	G	C	0.58 (1KG)	OR (GG/CG+CC)=2.13	1.031–4.397	0.036
G3 / G1, G2	2002	Wang et al. [18]	UBC	UC	Japanese	80 (G3) /138 (G2+G1)	G870A(rs9344)	11q13.3	CCND1	A	G	0.6 (Cases) /	OR (A/G)=1.77	1.16-2.69	0.008

											0.45 (Controls) / 0.41 (1KG)				
G3 / G1+G2	2012	Kucukgergin et al. [19]	UBC	UC	Turkish	70 (G3) / 72 (G1+G2)	CCR2 V64I (rs1799864)	3p21.31	CCR2	A	G	0.15 (1KG)	OR (AA/GG)=3.09 OR (AG+AA/GG)=1.58	1.02–9.34 1.07–2.32	0.045 0.020
G3 / G1+G2	2014	Zhou et al. [20]	UBC (excluding Tis)	UC	Chinese	188 (G3) / 104 (G1+G2)	rs3756712	5p15.33	PDCD6	G	T	0.40 (1KG)	OR (GT/TT+GG)=2.38 OR (GG/GT+TT)=3.57 OR (TT+GG/GG)=1.89	1.35–4.17 1.03–12.50 1.05–3.33	<0.05
G3 / G1+G2	2014	Zhou et al. [20]	UBC (excluding Tis)	UC	Chinese	188 (G3) / 104 (G1+G2)	rs4957014	5p15.33	PDCD6	G	T	0.65 (1KG)	OR (GT+GG/TT)=1.92	1.14–3.33	<0.05
G3 / G1+G2	2016	Gautam et al. [21]	UBC	UC	Indo-European (Caucasian)	47 (G3) / 185 (G1+G2)	'-174G>C (rs1800795)	7p15.3	IL6	C	G	0.14 (1KG)	Chi-square = 10.59	N/A	0.032
G3 / Healthy controls	2014	Gu et al. [22]	UBC	Not reported	Chinese	117 (G3) / 670 (Healthy subjects)	696 C/T (rs2664139)	15q14	TSP-1 (THBS1)	C	T	0.43 (1KG)	OR (CC/TT+CT)=1.84	1.00-3.36	0.049
G3 / Healthy controls	2017	Ali et al. [8]	UBC	UC	Pakistani	67 (High grade) / 200 (Healthy controls)	rs1801282	3p25.2	PPARG	G	C	0.19 (Cases) / 0.12 (Controls) / 0.07 (1KG)	OR (GG/CC)=5.97	1.3–26	<0.05
High grade (G2+G3+G	2007	Sanyal et al. [23]	UBC	Not reported	European (Sweden)	150 (High grade) / 110 (Low grade)	G39E (rs1042821)	2p16.3	MSH6	A	G	0.20 (1KG)	RR (AG+AA/GG)=1.7	1.0-3.0	0.05

4) / Low grade (G1+G2A)															
High grade (G2B+G3) NMIBC / Low grade (G1+G2A) NMIBC (patients ≤71 years)	2006	Sakano et al. [14]	NMIBC	UC	European (Sweden)	56 (High grade) / 60 (Low grade)	Asp1104His (rs17655)	13q33.1	XPG (ERCC5)	C	G	0.36 (1KG)	OR (GC+CC/GG)=3.3	1.5-7.3	0.003
G2+G3	2018	Ahmed et al. [9]	UBC	UC	Pakistani	54 (High grade UBC) / 99 (Controls)	rs2304277	3p25.3	OGG1	G	A	0.65 (1KG)	OR (GG/AA)=3.45	1.52–7.80	<0.05
G2+G3	2018	Ahmed et al. [9]	UBC	UC	Pakistani	72 (High grade UBC) / 184 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (AC/AA)=2.81	1.48–5.33	<0.05
G2+G3	2018	Ahmed et al. [9]	UBC	UC	Pakistani	57 (High grade UBC) / 167 (Controls)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (CC/AA)=2.58	1.09-6.11	<0.05
G2+G3	2018	Ahmed et al. [9]	UBC	UC	Pakistani	166 (High grade UBC) / 400 (Controls) (Allele count instead of individuals)	rs2228001	3p25.1	XPC	C	A	0.32 (1KG)	OR (C/A)=1.86	1.27-2.73	<0.05
G3+G4 / G1+G2	2010	Pandith et al. [24]	UBC	UC + 1 adenocarcinoma	Indian	56 (G3+G4)/ 52 (G1+G2)	Arg72Pro (rs1042522)	17p13.1	TP53	C	G	0.54 (1KG)	OR (CC+CG/GG)=4.6	1.4-15.6	0.005

CI-confidence interval; EA-effect allele; EAF-effect allele frequency; MIBC-muscle-invasive bladder cancer; NMIBC-non-muscle-invasive bladder cancer; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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242 Supplementary Table 6. Summary associations for previously reported SNPs on urinary bladder cancer risk group at the time of diagnosis.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
Associations for low-risk bladder cancer:															
Associations reducing the risk of low-risk bladder cancer:															
Low-risk (TaG2)	2007	Sanyal et al. [1]	UBC	Not reported	European (Sweden)	31 (AG+AA) / 95 (GG)	G39E (rs1042821)	2p16.3	MSH6	A	G	0.20 (1KG)	RR (AG+AA/GG)=0.7	0.5-0.9	0.009
Low-risk (TaG2)	2007	Sanyal et al. [2]	UBC	Not reported	European (Sweden)	28 (CT+TT) / 98 (CC)	P187S (rs1800566)	16q22.1	NQO1	T	C	0.29 (1KG)	RR (CT+TT/CC)=0.7	0.5-0.9	0.005
Associations increasing the risk of low-risk bladder cancer:															
Low-risk (TaG1)	2007	Sanyal et al. [1]	UBC	Not reported	European (Sweden)	9 (TC+CC) / 2 (TT)	H27H (rs17350793)	11p15.5	HRAS	C	T	0.30 (1KG)	RR (TC+CC/TT)=5.0	1.1-22.2	0.02
Low-risk NMIBC (Ta+G1/G2)	2009	Wang et al. [3]	NMIBC	UC	Chinese	345 (Low-risk) / 465 (Healthy controls)	rs9642880	8q24.21	CASC11	T	G	0.54 (1KG)	OR(TG+TT/GG)=1.71	1.28-2.29	0.0002
Low-risk NMIBC (Ta+G1/G2)	2009	Stern et al. [4]	NMIBC (Ta+G1-2)	UC	Caucasian (Northern American)	274 (Low-risk) / 578 (Healthy controls)	rs710521	3q28	TP63	A	G	0.80 (1KG)	OR (A/G)=1.49	1.17-1.91	0.002
Low-risk NMIBC (Ta+G1/G2) / High-risk (Tis/T1/G3)	2010	Kiemeney et al. [5]	UBC	UC	European (multiple)	1559 (Low-risk) / 1875 (High-risk)	rs798766	4p16.3	TACC3/FGFR3	T	C	0.25 (Low-risk) / 0.22 (High-risk) / 0.24 (1KG)	OR (T)=1.17	1.04-1.31	0.009
Associations for high-risk bladder cancer:															
Associations reducing the risk of high-risk bladder cancer:															

High-risk NMIBC (TaG2-3+T1G1-3/ TaG1)	2010	Gangwar et al. [6]	UBC	UC	Indian	64 (High-risk NMIBC) / 25 (TaG1)	T309G (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	OR (GG/TT)=0.22	0.07-0.65	0.006
TaG2-G3+T1G1-G3 / TaG1	2013	Jaiswal et al. [7]	NMIBC	UC	Indian	106 (High-risk) / 33 (Low-risk)	IL18(−607) C/A (rs1946518)	11q23.1	IL18	A	C	0.41 (1KG)	OR (CA/CC)=0.44	0.19-0.97	0.042
TaG2-G3+T1G1-G3 / TaG1	2013	Jaiswal et al. [7]	NMIBC	UC	Indian	109 (High-risk) / 36 (Low-risk)	IL18(−137) G/C (rs187238)	11q23.1	IL18	C	G	0.79 (1KG)	OR (GC/GG)=0.50	0.22-1.12	0.042
High-risk NMIBC (TaG2-3+T1G1-3/ TaG1)	2009	Gangwar et al. [8]	NMIBC	UC	Indian	91 (High-risk NMIBC) / 34 (TaG1)	1263A>G (rs 4645978)	1p36.21	CASP9	G	A	0.42 (1KG)	OR (AG/AA)=0.39	0.15-0.96	0.042
High-risk NMIBC (TaG2-G3 + T1G1-3) / Low-risk NMIBC (TaG1)	2011	Jaiswal et al. [9]	NMIBC	Not reported	Indian	112 (High-risk) / 37 (Low-risk)	p53 codon 248 (rs11540652) A/C/G/T	17p13.1	TP53	A/C/T	G	T=0.00003 (TOPMED)	OR ((Arg/Trp, Arg/Gln) + (Trp/Trp, Arg/Arg))=0.32 ARG-G/GLN-A	0.15-0.69	0.003
G2+G3 with T1-T4 / G1+G2 with Ta	2011	Ratanajaraya et al. [10]	UBC	Not reported	Japanese	207 (Invasive) / 171 (Non-invasive)	rs17650301	17q23.3	POLG2	C	A	0.39 (Cases) / 0.29 (Controls) / 0.14 (1KG)	OR (A/C)=1.53	1.13 – 2.08	9.50E-03
High grade NMIBC (Ta+G3/T1+G2/ T1+G3)	2009	Guey et al. [11]	NMIBC	UC	European (Spain)	219 (Only reported overall)	rs1801406	13q13.1	BRCA2	G?	A/C?	G=0.27 (1KG)	OR (G?/A?C?)=1.36	1.08-1.72	0.01
High grade NMIBC (TaG3+T1G2-3)	2009	Guey et al. [11]	NMIBC	UC	European (Spain)	219 (Only reported overall)	rs828702	2q35	XRCC5	G	A	0.45 (1KG)	OR (G/A)=1.28	1.03-1.58	0.026
High-risk (TaG3+T1)	2007	Sanyal et al. [1]	UBC	Not reported	European (Sweden)	25 (AG+AA) / 31 (GG)	G39E (rs1042821)	2p16.3	MSH6	A	G	0.20 (1KG)	RR (AG+AA/GG)=1.8	1.1-2.9	0.02

High-risk NMIBC (TaG2-3+T1G1-3) / Healthy controls	2009	Gangwar et al. [12]	UBC	UC	Indian	60 (High-risk NMIBC) / 139 (Heathy controls)	rs1052133	3p25.3	OGG1	G	C	0.30 (1KG)	OR (GG/TT)=2.46	1.1.0-5.48	0.027
High-risk NMIBC (TaG2-3+T1G1-3) / Healthy controls	2009	Gangwar et al. [12]	NMIBC	UC	Indian	59 (High-risk NMIBC) / 196 (Heathy controls) 63 (High-risk NMIBC) / 134 (Healthy controls) 59 (High-risk NMIBC) / 196 (Healthy controls)	rs7003908	8q11.21	XRCC7 (PRKDC)	G	T	0.33 (1KG)	OR (GT/TT)=3.38 OR (GG/TT)=8.00 OR (GG/GT+TT)=3.16	1.61-7.06 3.74-17.10 1.94-5.13	0.001 <0.001 <0.001
High-risk NMIBC (TaG2-3+T1G1-3/ TaG1)	2010	Gangwar et al. [6]	UBC	UC	Indian	73 (High-risk NMIBC) / 16 (TaG1)	G870A (rs9344)	11q13.3	CCND1	A	G	0.41 (1KG)	OR (AA/GG)=4.55	1.34-15.4	0.015

CI-confidence interval; EA-effect allele; EAF-effect allele frequency; MIBC-muscle-invasive bladder cancer; NMIBC-non-muscle-invasive bladder cancer; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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281 Supplementary Table 7. Summary associations for previously reported SNPs on urinary bladder cancer recurrence.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
Associations reducing the risk of bladder cancer recurrence:															
NMIBC recurrence (non-BCG-treated)	2005	Leibovici et al. [1]	NMIBC	Not reported	Caucasian (White)	60 (Recurrence) / 29 (No recurrence)	Pro12Ala (rs1801282)	3p25.2	PPARG	G	C	0.07 (1KG)	HR (CG+GG/CC)=0.41	0.20-0.86	<0.05
NMIBC recurrence (<64 year-old group)	2006	Zhao et al. [2]	NMIBC	UC + Other	Caucasian (Northern American)	48 (Recurrence) / 51 (No recurrence)	Pro198Leu (rs1050450)	3p21.31	GPX1	T	C	0.22 (1KG)	HR (CT+TT/CC)=0.37	0.20-0.70	<0.05
NMIBC recurrence (BCG-treated)	2006	Lin et al. [3]	NMIBC (BCG-treated)	UC + Other	Caucasian (Northern American)	18 (Recurrence) / 30 (No recurrence)	C160A (rs16260)	16q22.1	CDH1	A	C	0.24 (1KG)	HR (AC+AA/CC)=0.21	0.07-0.63	<0.05
NMIBC recurrence (BCG-treated)	2008	Ahirwar et al. [4]	NMIBC (BCG-treated)	Not reported	Indian	22 (Recurrence) / 33 (No recurrence)	174G/C (rs1800795)	7p15.3	IL6	C	G	0.14 (1KG)	HR (CC/GG)=0.298	0.09-0.91	0.03
NMIBC Recurrence (TUR-treated)	2009	Horikawa et al. [5]	NMIBC	UC	Japanese	49 (Recurrence) / 38 (No recurrence)	Arg72Pro (rs1042522)	17p13.1	TP53	C	G	0.54 (1KG)	HR (CC/CG+GG)=0.36	0.14-0.93	0.035
NMIBC recurrence (BCG-treated)	2009	Ahirwar et al. [6]	NMIBC	UC	Indian	19 (Recurrence) / 32 (No recurrence)	1031T>C (rs1799964)	6p21.33	TNFA	C	T	0.22 (1KG)	HR (CC/TT)=0.38	0.14-0.98	0.024
NMIBC recurrence (BCG-treated)	2009	Gangwar et al. [7]	NMIBC	UC	Indian	20 (Recurrence) / 32 (No recurrence)	1263A>G (rs4645978)	1p36.21	CASP9	G	A	0.42 (1KG)	HR (GG/AA)=0.22	0.62-0.75	0.005

NMIBC Recurrence (BCG-treated)	2009	Gangwar et al. [8]	UBC	UC	Indian	20 (Recurrence) / 27 (No recurrence)	rs7003908	8q11.21	XRCC7 (PRKDC)	G	T	0.33 (1KG)	HR (GG/TT)=0.25	0.09-0.65	0.004
NMIBC Recurrence (BCG-treated)	2010	Gangwar et al. [9]	NMIBC	UC	Indian	21 (Recurrence) / 26 (No recurrence)	T309G (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	HR (GG/TT)=0.25	0.08-0.80	0.019
UBC Recurrence (BCG-treated)	2010	Ahirwar et al. [10]	UBC	Not reported	Indian	22 (Recurrence) / 32 (No recurrence)	rs4073	4q13.3	IL8 (CXCL8)	A	T	0.52 (1KG)	HR (AA/TT)=0.12	0.04-0.41	<0.001
NMIBC Recurrence (BCG-treated)	2012	Jaiswal et al. [11]	NMIBC	Not reported	Indian	32 (Recurrence) / 31 (No recurrence) 25 (Recurrence) / 26 (No recurrence)	Survivin 31G>C (rs9904341)	17q25.3	Survivin (BIRC5)	C	G	0.39 (1KG)	HR (CG/GG)=0.35 HR (CC/GG)=0.22	0.16-0.77 0.05-0.95	0.009 0.043
NMIBC Recurrence (BCG-treated)	2012	Wei et al. [12]	NMIBC	UC	Caucasian (Northern American)	110 (Recurrence) / 82 (No recurrence)	rs804267	8p23.1	NEIL2	C	T	0.31 (1KG)	HR (CT/TT)=0.53	0.36–0.78	0.001
NMIBC Recurrence (BCG-treated)	2012	Wei et al. [12]	NMIBC	UC	Caucasian (Northern American)	110 (Recurrence) / 82 (No recurrence)	rs8191604	8p23.1	NEIL2	C	A	0.18 (1KG)	HR (CA/AA)=0.54	0.36–0.81	0.003
NMIBC Recurrence	2012	Wang et al. [13]	NMIBC	UC	Chinese	74 (Recurrence) / 125 (No recurrence)	rs2910164	5q33.3	MIR146A	C	G	0.28 (ExAC)	(HR (GC+CC/GG)=0.58	0.36–0.94	0.016
NMIBC Recurrence (TUR-treated)	2013	Ke et al. [14]	NMIBC (TUR-treated)	Not reported	Caucasian (Northern American)	91 (Recurrence) / 45 (No recurrence)	rs197412	1p13.2	DDX20	T	C	0.53 (1KG)	HR (TT+TC/CC)= 0.58	0.40–0.82	0.002

NMIBC Recurrence	2013	Lee et al. [15]	NMIBC	UC	Caucasian (Northern American)	232 (Recurrence) / 189 (No recurrence)	rs511918	1q25.3	RGS16	T	G	0.47 (1KG)	HR (T/G)=0.81	0.66-0.99	0.0381
NMIBC Recurrence	2013	Lee et al. [15]	NMIBC	UC	Caucasian (Northern American)	232 (Recurrence) / 189 (No recurrence)	rs16829458	1q31.2	RGS2	A	G	0.12 (1KG)	HR (AG/GG)=0.63	0.41-0.95	0.0268
NMIBC Recurrence	2013	Lee et al. [15]	NMIBC	UC	Caucasian (Northern American)	232 (Recurrence) / 189 (No recurrence)	rs3795617	1q31.2	RGS13	A	G	0.38 (1KG)	HR (A/G)=0.79	0.65-0.96	0.0187
NMIBC Recurrence	2014	Zhang et al. [16]	NMIBC	UC	Chinese	28 (AT) / 297 (TT)	rs2505568	7q22.3	NAMPT	A	T	0.57 (1KG)	HR (AT/TT)=0.30	0.09–0.97	0.03 (log-rank)
UBC Recurrence	2014	Zhang et al. [16]	UBC	UC	Chinese	95 (Recurrence) / 230 (No recurrence)	rs2505568	7q22.3	NAMPT	A	T	0.57 (1KG)	OR (AT/TT)=0.25	0.07–0.86	<0.05
NMIBC Recurrence (TUR- and BCG-treated)	2015	Lima et al. [17]	NMIBC after TUR+BCG	Not reported	European (Southern Portugal)	70 (Recurrence) / 134 (No recurrence)	rs391835	3p21.31	CCR2	A	G	0.41 (1KG)	HR (AA/GG)=0.410 HR (GA+AA/GG)=0.455	0.191–0.879 0.232–0.893	0.022 0.022
NMIBC Recurrence (TUR-treated + Epirubicin)	2015	Deng et al. [18]	UBC (TUR- and Epirubicin-treated)	Not reported	Chinese	49 (Recurrence) / 75 (No recurrence) 50 (Recurrence) / 80 (No recurrence)	rs2854509	19q13.31	XRCC1	A	C	0.82 (1KG)	HR (AC/CC)=0.24 HR (AC+AA/CC)=0.23	0.10–0.57 0.10–0.53	0.036 (log-rank) 0.010 (log-rank)
NMIBC Recurrence (TUR-treated + Epirubicin)	2015	Deng et al. [18]	UBC (TUR- and Epirubicin-treated)	Not reported	Chinese	48 (Recurrence) / 77 (No recurrence) 50 (Recurrence) / 80 (No recurrence)	rs3213255	19q13.31	XRCC1	C	T	0.32 (1KG)	HR (CT/TT=0.17 HR (CT+CC/TT)=0.17	0.58–0.50 0.06–0.46	0.001 (log-rank) 0.001 (log-rank)
High-risk NMIBC Recurrence	2015	Ryk et al. [19]	High-risk (either TaG3, T1, TaG1+conC	UC	European (Sweden)	5 (TT, BCG-treated) / 12 (TT, not BCG-treated)	rs2070744	7q36.1	NOS3	T	C	0.77 (1KG)	HR (BCG-reated TT/Not BCG-treated TT)=0.23	0.08–0.70	0.009

(BCG-treated)			IS,TaG2+conCIS or primary CIS) NMIBC (treated with BCG)												
High-risk NMIBC Recurrence (BCG-treated)	2015	Ryk et al. [19]	High-risk (either TaG3, T1, TaG1+conCIS,TaG2+conCIS or primary CIS) NMIBC (treated with BCG)	UC	European (Sweden)	17 (TT, BCG-treated) / 15 (TT, not BCG-treated)	rs2070744	7q36.1	NOS3	T	C	0.77 (1KG)	HR (BCG-reated CT+CC/Not BCG-treated CT+CC)=0.25	0.11–0.54	<0.001
High-risk NMIBC Recurrence (BCG-treated)	2015	Ryk et al. [19]	High-risk (either TaG3, T1, TaG1+conCIS,TaG2+conCIS or primary CIS) NMIBC (treated with BCG)	UC	European (Sweden)	7 (GG, BCG-treated) / 9 (GG, not BCG-treated)	rs1799983	7q36.1	NOS3	G	T	0.82 (1KG)	HR (BCG-reated GG/Not BCG-treated GG)=0.29	0.10–00.87	0.028
NMIBC Recurrence	2015	Xie et al. [20]	NMIBC	UC	Chinese	62 (Recurrence) / 259 (No recurrence)	SNP309 T>G (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	OR (TG/TT)=0.562	0.338-0.933	0.026
NMIBC Recurrence	2015	Xie et al. [20]	NMIBC	UC	Chinese	49 (Recurrence) / 178 (No recurrence)	SNP309 T>G (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	OR (GG/TT)=0.501	0.279-0.900	0.021

NMIBC Recurrence	2015	Xie et al. [20]	NMIBC	UC	Chinese	81 (Recurrence) / 362 (No recurrence)	SNP309 T>G (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	OR (TG+GG/TT)=0.531	0.336-0.839	0.007
NMIBC Recurrence (Epirubicin-treated)	2015	Li et al. [21]	NMIBC (Epirubicin-treated)	UC	Chinese	47 (Recurrence) / 78 (No recurrence)	rs915927	19q13.2	XRCC1	G	A	0.32 (1KG)	HR (AG/AA)=0.21	0.08-0.53	0.02
NMIBC Recurrence (Epirubicin-treated)	2015	Li et al. [21]	NMIBC (Epirubicin-treated)	UC	Chinese	48 (Recurrence) / 81 (No recurrence)	rs915927	19q13.2	XRCC1	G	A	0.32 (1KG)	HR (AG+GG/AA)=0.24	0.10-0.59	0.009
NMIBC Recurrence (Epirubicin-treated)	2015	Li et al. [21]	NMIBC (Epirubicin-treated)	UC	Chinese	46 (Recurrence) / 78 (No recurrence)	rs2854501	19q13.2	XRCC1	T	C	0.18 (1KG)	HR (CT/CC)=0.10	0.03-0.35	0.002
NMIBC Recurrence (Epirubicin-treated)	2015	Li et al. [21]	NMIBC (Epirubicin-treated)	UC	Chinese	48 (Recurrence) / 81 (No recurrence)	rs2854501	19q13.2	XRCC1	T	C	0.18 (1KG)	HR (CT+TT/CC)=0.16	0.06-0.43	0.001
Associations increasing the risk of bladder cancer recurrence:															
NMIBC Recurrence	2005	Kim et al. [22]	NMIBC	UC	Korean	38 (Recurrence) / 55 (No recurrence)	Ser326Cys (rs1052133)	3p25.3	OGG1	G	C	0.30 (1KG)	OR (CG+GG/CC)=6.49	1.25-33.3	0.026
NMIBC recurrence (BCG-treated)	2005	Gu et al. [23]	NMIBC (BCG-treated)	Not reported	Caucasian (Northern American)	121 (Recurrence) / 77 (No recurrence)	Met1097Val (rs2228526)	10q11.23	ERCC6	C	G	0.18 (1KG)	HR (CG+CC/GG)=1.54	1.02-2.33	<0.05
NMIBC recurrence (maintenance BCG-treated)	2005	Leibovici et al. [1]	NMIBC (BCG-treated)	Not reported	Caucasian (White)	12 (Recurrence) / 16 (No recurrence) 8 (Recurrence) / 10 (No recurrence) 16 (Recurrence) /	174G/C (rs1800795)	7p15.3	IL6	C	G	0.14 (1KG)	HR (GC/GG)=4.31 HR (CC/GG)=5.47 HR (CG+CC/GG)=4.60	1.09-17.09 1.05-28.44 1.24-17.09	<0.05 <0.05 <0.05

						17 (No recurrence)									
NMIBC recurrence (BCG-treated)	2006	Decobert et al. [24]	NMIBC (BCG-treated)	Not reported	Caucasian (Canadian)	51 (Recurrence) / 16 (No recurrence)	D543N (rs17235409)	2q35	NRAMP1 (SLC11A1)	A	G	0.07 (1KG)	HR (AG/GG)=5.74	2.4-13.8	<0.001
NMIBC recurrence (BCG-treated)	2008	Mittal et al. [25]	NMIBC	UC	Indian	19 (Recurrence) / 16 (No recurrence)	Codon 194 (rs1799782)	19q13.2	XRCC1	T	C	0.12 (1KG)	OR (CT/CC)=4.57	1.10-18.97	0.03
NMIBC recurrence (BCG-treated)	2008	Mittal et al. [25]	NMIBC (BCG-treated)	UC	Indian	10 (recurrence) / 15 (No recurrence)	Codon 399 (rs25487)	19q13.2	XRCC1	A	G	0.26 (1KG)	HR (AA/GG)=5.05	1.34-19.01	0.01
NMIBC recurrence (BCG-treated)	2009	Gangawar et al. [26]	NMIBC	Not reported	Indian	27 (Recurrence) / 19 (No recurrence)	Asp312Asn (G>A) (rs1799793)	19q13.3	ERCC2	A	G	0.19 (1KG)	HR(AA/GG)=3.07	1.22-7.68	0.016
NMIBC recurrence (BCG-treated)	2009	Ahirwar et al. [27]	NMIBC	UC	Indian	21 (Recurrence) / 29 (No recurrence) 23 (Recurrence) / 23 (No Recurrence)	rs2430561	12q15	IFN-G	A	T	0.28 (1KG)	HR (TA/TT)=2.80 HR (A/T)=2.24	1.13-6.97 1.06-5.80	0.024 0.036
NMIBC Recurrence (non-BCG-treated)	2009	Gangwar et al. [8]	UBC	UC	Indian	20 (Recurrence) / 23 (No recurrence)	rs1052133	3p25.3	OGG1	G	C	0.30 (1KG)	HR (GG/TT)=4.04	1.33-12.1	0.013
NMIBC Recurrence (BCG-treated)	2010	Gangwar et al. [28]	NMIBC	UC	Indian	14 (Recurrence) / 27 (No recurrence) 28 (recurrence) / 49 (No recurrence)	Lys939Gln (rs2228001)	3p25.1	XPC	C	A	0.32 (1KG)	HR (CC/AA)=3.21 HR (AC+CC/AA)=3.98	1.07-9.61 1.02-10.7	0.036 <0.05

Low-risk NMIBC recurrence	2010	Wang et al. [29]	NMIBC	UC	Chinese	24 (Recurrence) / 24 (No recurrence)	XPF 357A>C (rs744154)	16p13.12	XPF (ERCC4)	C	A	0.22 (1KG)	HR (AC+CC/AA)=3.62	1.42-9.28	<0.05
Low-risk NMIBC recurrence	2010	Kiemeney et al. [30]	UBC	UC	European (multiple)	305 (Recurrence) / 358 (No recurrence) 322 (Recurrence) / 375 (No recurrence)	rs798766	4p16.3	TACC3/FGFR3	T	C	0.25 (All low-risk NMIBC) / 0.24 (1KG)	HR (CT/CC)=1.31 HR (T/C)=1.23	1.04-1.64 1.04-1.47	0.020 0.019
NMIBC Recurrence (BCG-treated)	2010	Chen et al. [31]	NMIBC	UC + Other	Caucasians (Northern American) + European (Spain) for replication	118 (Recurrence) / 83 (No recurrence)	rs6463089	7p14.1	GLI3	A	G	0.09 (1KG)	HR (AG+AA/GG)=2.40	1.50-3.84	2.00E-04
NMIBC Recurrence (BCG-treated)	2010	Chen et al. [31]	NMIBC	UC + Other	Caucasians (Northern American) + European (Spain) for replication	117 (Recurrence) / 83 (No recurrence)	rs3801192	7p14.1	GLI3	A	G	0.07 (1KG)	HR (AG+AA/GG)=2.54	1.47-4.39	9.00E-04
NMIBC Recurrence (TUR-treated)	2010	Chen et al. [31]	NMIBC	UC + Other	Caucasians (Northern American) + European (Spain) for replication	230 (Recurrence) / 272 (No recurrence)	rs1233560	7q36.3	SSH	G	A	0.46 (1KG)	HR (G/A)=1.39	1.14-1.70	0.001
NMIBC Recurrence (TUR-treated)	2010	Chen et al. [31]	NMIBC	UC + Other	Caucasians (Northern American) + European (Spain) for replication	230 (Recurrence) / 272 (No recurrence)	rs11685068	2q14.2	GLI2	A	G	0.06 (1KG	HR (AG+AA/GG)=2.07	1.33-3.21	0.0013

NMIBC Recurrence (BCG-treated)	2010	Chiong et al. [32]	NMIBC (BCG-treated)	UC	Chinese	19 (Recurrence) / 4 (No recurrence)	D543N (rs17235409)	2q35	NRAMP1 (SLC11A1)	G	A	0.93 (1KG)	HR (GG/AG)=3.0	1.03–8.9	0.033
NMIBC Recurrence (BCG-treated)	2011	Srivastava et al. [33]	NMIBC (BCG-treated)	UC	Indian	31 (Recurrence) / 41 (No recurrence) 34 (Recurrence) / 44 (No recurrence)	rs243865	16q12.2	MMP2	C	T	0.86 (1KG)	HR (CT/CC)=4.32 HR (CT+TT/CC)=2.06	1.51–12.39 1.01–4.18	0.006 0.047
NMIBC Recurrence -(BCG-treated)	2012	Wei et al. [12]	NMIBC	UC	Caucasian (Northern American)	110 (Recurrence) / 82 (No recurrence)	rs804256	8p23.1	NEIL2	C	T	0.26 (1KG)	HR (CC/CT+TT)=4.58	2.61–8.02	1.00E-07
NMIBC Recurrence (BCG-treated)	2012	Wei et al. [12]	NMIBC	UC	Caucasian (Northern American)	110 (Recurrence) / 82 (No recurrence)	rs804276	8p23.1	NEIL2	G	A	0.62 (1KG)	HR (GG/AG+AA)=2.71	1.75–4.20	9.00E-06
NMIBC Recurrence (BCG-treated)	2012	Wei et al. [12]	NMIBC	UC	Caucasian (Northern American)	110 (Recurrence) / 82 (No recurrence)	rs4639	8p23.1	NEIL2	G	A	0.47 (1KG)	HR (GG/AG+AA)=2.60	1.68–4.03	2.00E-05
NMIBC Recurrence (BCG-treated)	2012	Wei et al. [12]	NMIBC	UC	Caucasian (Northern American)	110 (Recurrence) / 82 (No recurrence)	rs2173962	21q22.11	SOD1	G	A	0.06 (1KG	HR (GA/AA)=2.45	1.42–4.23	0.001
NMIBC Recurrence (TUR-treated)	2013	Ke et al. [14]	NMIBC (TUR-treated)	Not reported	Caucasian (Northern American)	91 (Recurrence) / 45 (No recurrence)	rs12186785	5p13.3	RNASEN (DROSHA)	C	T	0.05 (1KG)	HR (CT/TT)= 2.15	1.25–3.68	0.005
NMIBC Recurrence (BCG-treated)	2013	Jaiswal et al. [34]	NMIBC (BCG-treated)	UC	Indian	32 (Recurrence) / 42 (No recurrence)	IL18(−137) G/C (rs187238)	11q23.1	IL18	C	G	0.79 (1KG)	HR (GC/GG)=2.35	1.09-5.10	0.030

NMIBC Recurrence	2013	Lee et al. [15]	NMIBC	UC	Caucasian (Northern American)	232 (Recurrence) / 189 (No recurrence)	rs11199005	10q26.11	RGS10	A	G	0.35 (1KG)	HR (AG/GG)=1.47	1.02-2.12	0.041
NMIBC Recurrence	2013	Lee et al. [15]	NMIBC	UC	Caucasian (Northern American)	232 (Recurrence) / 189 (No recurrence)	rs1323291	1q31.2	RGS1	C	A	0.15 (1KG)	HR (CA/AA)=1.60	1.13-2.28	0.0084
NMIBC Recurrence	2014	Andrew et al. [35]	NMIBC	UC + Other	Caucasian (Northern American)	279 (Recurrence) / 248 (No recurrence) (but not presented for NMIBC group)	rs5742714	12q23.2	IGF1	C	G	0.9 (1KG)	HR (GC/GG)=1.61	1.19-2.17	0.002 (log-rank)
NMIBC Recurrence	2014	Andrew et al. [35]	NMIBC	UC + Other	Caucasian (Northern American)	279 (Recurrence) / 248 (No recurrence) (but not presented for NMIBC group)	rs2238151	12q24.12	ALDH2	C	T	0.7 (1KG)	HR (CC/TT)=1.94	1.32-2.85	<0.001 (log-rank)
MIBC Recurrence	2014	Zhou et al. [36]	MIBC	UC	Chinese	47 (Recurrence) / 156 (No recurrence)	rs4957014	5p15.33	PDCD6	G	T	0.65 (1KG)	HR (GT/TT+GG)=1.93	1.08-3.45	0.03
NMIBC Recurrence (TUR- and BCG-treated)	2015	Lima et al. [17]	NMIBC after TUR+BCG	Not reported	European (Southern Portugal)	70 (Recurrence) / 134 (No recurrence)	rs5498	19p13.2	ICAM1	G	A	0.36 (1KG)	HR (GG/AA+AG)=1.76	1.050–2.949	0.032
NMIBC Recurrence (TUR- and BCG-treated)	2015	Lima et al. [17]	NMIBC after TUR+BCG	Not reported	European (Southern Portugal)	70 (Recurrence) / 134 (No recurrence)	rs2275913	6p12.2	IL17A	A	G	0.29 (1KG)	HR (AA/GG+AG)=2.097	1.118–3.933	0.021
NMIBC Recurrence (TUR- and BCG-treated)	2015	Lima et al. [17]	NMIBC after TUR+BCG	Not reported	European (Southern Portugal)	70 (Recurrence) / 134 (No recurrence)	rs1799964	6p21.33	TNFA	C	T	0.22 (1KG)	HR (CC/TT+TC)=2.427	1.144–5.149	0.021

NMIBC Recurrence (TUR- and BCG-treated)	2015	Lima et al. [17]	NMIBC after TUR+BCG	Not reported	European (Southern Portugal)	70 (Recurrence) / 134 (No recurrence)	rs13278062	8p21.3	TRAILR1 (TNFRSF10A)	G	T	0.6 (1KG)	HR (TG/TT)=3.546 HR (GG/TT)=3.078 HR (TG+GG/TT)=3.195	1.477–8.513 1.251–7.573 1.373–7.433	0.005 0.014 0.007
NMIBC Recurrence (TUR- and BCG-treated)	2015	Ke et al. [37]	NMIBC (treated with TUR)	UC	Caucasians (European decent)	88 (Recurrence) / 45 (No recurrence)	rs3746162	19p13.3	GPX4	A	G	0.2 (Cases) / 0.21 (Controls) / 0.16 (1KG)	HR (AA/AG+GG)=5.43	2.19–13.46	0.0003
NMIBC Recurrence (TUR- and BCG-treated)	2015	Ke et al. [37]	NMIBC (TUR+BCG-treated)	UC	Caucasians (European decent)	110 (Recurrence) / 81 (No recurrence)	rs7265992	20q11.22	GSS	A	G	0.60 (Cases) / 0.62 (Controls) / 0.19 (1KG)	HR (AA/AG+GG)=3.43	1.56–7.56	0.002
NMIBC Recurrence (TUR- and BCG-treated)	2015	Ke et al. [37]	NMIBC (TUR+BCG-treated)	UC	Caucasians (European decent)	110 (Recurrence) / 81 (No recurrence)	rs6060124	20q11.22	GSS	A	C	0.61 (Cases) / 0.69 (Controls) / 0.26 (1KG)	HR (AA/AG+GG)=2.80	1.44–5.47	0.003
NMIBC Recurrence (TUR- and BCG-treated)	2015	Ke et al. [37]	NMIBC (TUR+BCG-treated)	UC	Caucasians (European decent)	110 (Recurrence) / 81 (No recurrence)	rs7260770	20q11.22	GSS	A	G	0.63 (Cases) / 0.69 (Controls) / 0.22 (1KG)	HR (AA/AG+GG)=2.56	1.34–4.90	0.005

NMIBC Recurrence (TUR- and BCG-treated)	2015	Ke et al. [37]	NMIBC (TUR+BCG-treated)	UC	Caucasians (European decent)	110 (Recurrence) / 81 (No recurrence)	rs4911455	20q11.22	GSS	C	A	0.62 (Cases) / 0.69 (Controls) / 0.28 (1KG)	HR (AA/AG+GG)=2.54	1.32–4.87	0.005
NMIBC Recurrence (BCG-treated)	2015	Deng et al. [38]	NMIBC (treated with intravesicular chemotherapy)	Not reported	Chinese	48 (Recurrence) / 76 (No recurrence) 24 (Recurrence) / 60 (No recurrence) 50 (recurrence) / 80 (No recurrence)	rs1695	11q13.2	GSTP1	G	A	0.35 (1KG)	HR (AG/AA)=3.29 HR (GG/AA)=5.18 HR (GG+AG/AA)=3.47	1.63–6.63 (AG/AA) 1.05–25.62 (GG/AA) 1.75–6.89 (GG+AG/AA)	0.002 (log-rank) 0.001 (log-rank, for AG+GG)
NMIBC Recurrence (BCG-treated)	2015	Deng et al. [38]	NMIBC (treated with intravesicular chemotherapy)	Not reported	Chinese	35 (Recurrence) / 55 (No recurrence) 60 (Recurrence) / 70 (No recurrence)	rs4925	10q25.1	GSTO1	A	C	0.1 (1KG)	HR (AA/CC)=3.23 HR (AC+AA/CC)=1.96	1.16-8.94 (AA/CC) 1.05–3.70 (AC+AA/CC)	0.019 (log-rank) 0.042 (log-rank, for AC+AA)
Recurrence	2016	Wang et al. [39]	UBC (not reported whether NMIBC/UBC)	Not reported	Chinese	74 (Recurrence) / 125 (No recurrence)	rs2042329	5q12.3	CWC27	T	G	0.18 / 0.34 (1KG)	HR (T/G)=1.54	1.10-2.16	0.012
MIBC recurrence	2018	Li et al. [40]	MIBC	Not reported	Chinese	42 (Recurrence) / 96 (No recurrence)	rs4758680	12q24.31	IL31	A	C	0.29 (1KG)	HR (CA+AA/CC)=2.02	1.06-3.85	0.03
MIBC recurrence	2018	Li et al. [40]	MIBC	Not reported	Chinese	42 (Recurrence) / 96 (No recurrence)	rs4758680	12q24.31	IL31	A	C	0.29 (1KG)	HR (CA/CC)=1.90	1.15-3.16	0.01

NMIBC Recurrence (BCG-treated)	2017	Williams et al. [41]	NMIBC	UC	Northern American (although n restriction on ethnicity were applied)	123 (Recurrence) / 82 (No recurrence)	rs3138056	14q13.2	NFKBIA	T?	C?	0.32 (Reported in the study) / T=0.38 (1KG)	HR(TT/CC)=3.26	1.83-5.8	6.20x10-5
NMIBC Recurrence (BCG-treated)	2018	Wang et al. [42]	NMIBC (BCG-treated)	UC	Chinese	63 (Recurrence) / 127 (No recurrence)	rs1544410	12q13.11	VDR	A	G	0.30 (1KG)	HR (AA+AG/GG)=3.95	Not reported	0.037
NMIBC Recurrence	2013	Yang et al. [43]	NMIBC	Not reported	Chinese	45 (Recurrence) / 100 (No recurrence)	TSP-1-1223 (rs2169830)	15q14	TSP-1 (THBS1)	G	A	0.42 (1KG)	HR (GG/AA)=2.63	1.43-4.83	0.002
NMIBC Recurrence	2013	Yang et al. [43]	NMIBC	Not reported	Chinese	45 (Recurrence) / 100 (No recurrence)	TSP-1-1223 (rs2169830)	15q14	TSP-1 (THBS1)	G	A	0.42 (1KG)	HR (AG+GG/AA)=1.95	1.20-3.19	0.007
NMIBC Recurrence	2013	Yang et al. [43]	NMIBC	Not reported	Chinese	45 (Recurrence) / 100 (No recurrence)	TSP-1-1223 (rs2169830)	15q14	TSP-1 (THBS1)	G	A	0.42 (1KG)	HR (GG/AG+AA)=2.07	1.23-3.49	0.006

BCG-Bacillus Calmette-Guérin; CI-confidence interval; CIS-carcinoma in situ; EA-effect allele; EAF-effect allele frequency; MIBC-muscle-invasive bladder cancer; NMIBC-non-muscle-invasive bladder cancer; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; TUR-transurethral resection; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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399 Supplementary Table 8. Summary associations for previously reported SNPs on urinary bladder cancer progression.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
Associations reducing the risk of bladder cancer progression:															
NMIBC Progression (increase in stage)	2007	Sanyal et al. [1]	UBC	Not reported	European (Sweden)	94 (TC+CC) / 102 (TT)	H27H (rs17350793)	11p15.5	HRAS	C	T	0.30 (1KG)	HR (TC+CC/TT)=0.3	0.1-0.9	0.03
UBC Progression (increase in stage)	2011	Ryk et al. [2]	UBC	Not reported	European (Sweden)	67 (Progression) / 215 (No progression)	rs2297518	17q11.2	NOS2	T	C	0.17 (1KG)	HR (TT/CC)=0.21	0.05–0.87	0.031
NMIBC Progression (transition from NMIBC to MIBC or metastatic cancer)	2013	Lee et al. [3]	NMIBC	UC	Caucasian (Northern American)	85 (Progression) / 336 (No progression)	rs10917690	1q23.3	RGS5	G	A	0.29 (1KG)	HR (G/A)=0.58	(0.39-0.86	0.0065
NMIBC Progression (transition from NMIBC to MIBC or metastatic cancer)	2013	Lee et al. [3]	NMIBC	UC	Caucasian (Northern American)	85 (Progression) / 336 (No progression)	rs4075958	5q35.3	RGS14	A	G	0.18 (1KG)	HR (A/G)=0.65	0.44-0.97	0.0332

NMIBC Progression (transition from NMIBC to MIBC or metastatic cancer)	2013	Lee et al. [3]	NMIBC	UC	Caucasian (Northern American)	85 (Progression) / 336 (No progression)	rs10926466	1q23.1	RGS7	T	C	0.63 (1KG)	HR (TC/CC)=0.60	0.36-0.98	0.0414
NMIBC Progression (transition from NMIBC to MIBC or metastatic cancer)	2013	Lee et al. [3]	NMIBC	UC	Caucasian (Northern American)	85 (Progression) / 336 (No progression)	rs12038803	1q23.1	RGS7	C/G/T? (Not reported)	A	0.66 (1KG)	HR (?A/AA)=0.60	0.36-0.98	0.0431
High-risk NMIBC Progression (BCG-treated) (transition from NMIBC to MIBC, metastatic cancer, or cancer-specific death)	2015	Ryk et al. [4]	High-risk (either TaG3, T1, TaG1+conCIS, TaG2+conCIS or primary CIS) NMIBC (treated with BCG)	UC	European (Sweden)	1 (TT, BCG-treated) / 11 (TT, not BCG-treated)	rs2070744	7q36.1	NOS3	T	C	0.77 (1KG)	HR (BCG-reated TT/Not BCG-treated TT)=0.05	0.01–0.42	0.005

High-risk NMIBC Progression (BCG-treated) (transition from NMIBC to MIBC, metastatic cancer, or cancer-specific death)	2015	Ryk et al. [4]	High-risk (either TaG3, T1, TaG1+conCIS, TaG2+conCIS or primary CIS) NMIBC (treated with BCG)	UC	European (Sweden)	3 (GG, BCG-treated) / 9 (GG, not BCG-treated)	rs1799983	7q36.1	NOS3	G	T	0.82 (1KG)	HR (BCG-reated GG/Not BCG-treated GG)=0.10	0.02–0.46	0.003
UBC Progression (metastases present)	2015	Deng et al. [5]	UBC	Not reported	Chinese	132 (metastasis) / 27 (no metastasis)	rs2910164	5q33.3	MIR146A	G	C	0.39 (all UBC) / 0.32 (TOPMED)	OR=0.45 (log-additive model)	0.21-0.93	0.025
Associations reducing the risk of bladder cancer progression:															
NMIBC Progression (increase in stage)	2003	Sakano et al. [6]	UBC	UC	European (Sweden)	33 (CT+TT) / 178 (CC)	540C>T (rs3088440)	9p21	CDKN2A	T	C	0.08 / 0.17 (1KG)	HR (CT+TT/CC)=2.5	1.0-6.1	0.043
NMIBC progression (BCG-treated) (increase in stage)	2006	Basturk et al.[7]	[7]NMIBC (BCG-treated)	UC	Turkish	59 (Progression) / 14 (No progression)	1082 (rs1800896)	1q32.1	IL10	G	A	0.27 (1KG)	OR (GG)=5.47	0.84-38.3	0.05
NMIBC progression (BCG-treated) (increase in stage)	2006	Basturk et al. [7]	NMIBC (BCG-treated)	UC	Turkish	59 (Progression) / 14 (No progression)	1098 (rs2243248)	5q31.1	IL4	G	T	0.11 (1KG)	OR (GG)=18.33	0.8-412.2	0.05

NMIBC progression (BCG-treated) (increase in stage)	2006	Basturk et al. [7]	NMIBC (BCG-treated)	UC	Turkish	59 (Progression) / 14 (No progression)	Codon 10T (rs1800470)	19q13.2	TGFB1	T	C	0.55 (1KG)	OR (T)=7.5	1.33-55.1	0.006
NMIBC progression (BCG-treated) (increase in stage)	2006	Basturk et al. [7]	NMIBC (BCG-treated)	UC	Turkish	59 (Progression) / 14 (No progression)	Codon 25G (rs1800471)	19q13.2	TGFB1	G	C	0.05 (1KG)	OR (G)=7.17	0.83-160.2	0.04
Progression (metastases present)	2012	Guirado et al. [8]	UBC	UC	European (Spain)	92 (Yes) / 136 (No)	rs9302752	16q12.1	NOD2	G	A	0.50 (1KG)	OR (GG/AG+AA)=3.23 OR (GG/AG)=3.16	1.25-8.33 1.12-8.33	0.011 0.022
NMIBC Progression (BCG-treated) (transition from NMIBC to MIBC or metastatic cancer)	2012	Wei et al. [9]	NMIBC	UC	Caucasian (Northern American)	75 (Progression) / 327 (No progression)	rs3890995	12q24.11	UNG	C	T	0.22 (1KG)	HR (CC+CT/TT,=1.92	1.33–2.77	0.0005
NMIBC Progression (TUR-treated) (transition from NMIBC to MIBC or metastatic cancer)	2013	Ke et al. [10]	NMIBC	Not reported	Caucasian (Northern American)	75 (Progression) / 324 (No progression)	rs720012	22q11.21	DGCR8	A	G	0.22 (1KG)	HR (AA/AG+GG)=3.97	1.52–10.36	0.005

NMIBC Progression (TUR-treated) (transition from NMIBC to MIBC or metastatic cancer)	2013	Ke et al. [10]	NMIBC	Not reported	Caucasian (Northern American)	75 (Progression) / 326 (No progression)	rs2073778	22q11.21	DGCR8	T	C	0.22 (1KG)	HR (TT/CT+CC= 4.00	1.53–10.46	0.005
NMIBC Progression (transition from NMIBC to MIBC or metastatic cancer)	2013	Lee et al. [3]	NMIBC	UC	Caucasian (Northern American)	85 (Progression) / 336 (No progression)	rs1323291	1q31.2	RGS1	C	A	0.15 (1KG)	HR (CA/AA)=2.14	1.25-3.66	0.0059
NMIBC Progression (transition from NMIBC to MIBC or metastatic cancer)	2013	Lee et al. [3]	NMIBC	UC	Caucasian (Northern American)	85 (Progression) / 336 (No progression)	rs6678136	1q23.3	RGS4	A	G	0.46 (1KG)	HR (AG/GG=2.07	1.20-3.57	0.0094

NMIBC Progression (transition from NMIBC to MIBC or metastatic cancer)	2013	Lee et al. [3]	NMIBC	UC	Caucasian (Northern American)	85 (Progression) / 336 (No progression)	rs11585883	1q23.3	RGS5	C	T	0.03 (1KG)	HR (CT/TT)=1.93	1.12-3.32	0.018
UBC Progression (metastases present)	2015	Deng et al. [5]	UBC	Not reported	Chinese	132 (metastasis) / 27 (no metastasis)	rs2910164	5q33.3	MIR146A	G	C	0.39 (all UBC) / 0.32 (TOPMED)	OR (CG+GG / CC)= 2.63	1.03–6.67	0.04
MIBC Progression (confirmed disease relapse)	2016	Xu et al. [11]	Stage 4 UBC (treated with platinum-based chemotherapy)	UC	Chinese	41 (Overall; death and progression counts not reported)	C118T (rs11615)	19q13.32	ERCC1	T	C	0.27 / 0.33 (1KG)	HR (CC/CT+TT)=1.83	1.12-2.99	0.016
UBC Progression (transition from NMIBC to MIBC, metastatic cancer, or cancer-specific death)	2017	Hess et al. [12]	UBC	UC	European (Germany)	179 (Overall, death and progression counts not reported)	rs1801018 (c.21G>A)	18q21.33	BCL2	A	G	0.53 / 0.76 (1KG)	HR (AA/GG)=3.08	1.16–8.16	0.024

BCG-Bacillus Calmette-Guérin; CI-confidence interval; CIS-carcinoma in situ; EA-effect allele; EAF-effect allele frequency; MIBC-muscle-invasive bladder cancer; NMIBC-non-muscle-invasive bladder cancer; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; TUR-transurethral resection; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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431 Supplementary Table 9. Summary associations for previously reported SNPs on overall and cancer-specific survival for urinary bladder cancer.

Outcome	Year	Study	Patient subgroup	Cancer subtype	Ethnic background	Sample size (Cases/Controls)	SNP	Locus	Gene	EA	RA	EAF	Effect Size	95% CI	p value
Associations for cancer-specific death:															
Associations reducing the risk of cancer-specific death:															
High-risk NMIBC Cancer-specific death (BCG-treated)	2015	Ryk et al. [1]	High-risk (either TaG3, T1, TaG1+conCIS,TaG2+conCIS or primary CIS) NMIBC (BCG-treated)	UC	European (Sweden)	2 (GG, BCG-treated) / 6 (GG, not BCG-treated)	rs1799983	7q36.1	NOS3	G	T	0.82 (1KG)	HR (BCG-treated GG/Not BCG-treated GG)=0.16	0.03–0.84	0.030
MIBC Cancer-specific death	2005	Leibovici et al. [2]	MIBC	Not reported	Caucasian (White)	105 (CG+CC) / 44 (GG)	174G/C (rs1800795)	7p15.3	IL6	C	G	0.14 (1KG)	HR (CG+CC/CC)=0.39	0.15-1.00	<0.05
MIBC Cancer-specific death (Radiotherapy-treated)	2012	Teo et al. [3]	MIBC (Radiotherapy-treated)	Not reported	European (United Kingdom)	139 (AG+GG) / 50 (AA)	rs7180135	15q15.1	RAD51	G	A	0.27 (1KG)	HR (AG+GG/AA)=0.52	0.31-0.87	0.01
UBC Cancer-specific death	2009	Shinohara et al. [4]	UBC	UC + Other	Japanese	77 (GT+GG) / 18 (TT)	SNP309 (rs2279744)	12q15	MDM2	G	T	0.37 (1KG)	RR (GT+GG/TT)=0.57	0.36-0.95	0.031
UBC Cancer-specific death	2012	Guirado et al. [5]	UBC	UC	European (Spain)	Not reported	rs4129009	4p14	TLR10	T	C	0.85 (1KG)	HR (TT/CT+CC)=0.49	Not reported	0.022
UBC Cancer-specific death	2007	Sanyal et al. [6]	UBC	Not reported	European (Sweden)	68 (Dead) / 198 (Alive)	A222V (rs1801133)	1p36.22	MTHFR	T	C	0.25 (1KG)	HR (CT+TT/CC)=0.5	0.3-0.9	0.03
Associations increasing the risk of cancer-specific death															

MIBC Cancer-specific death	2009	Castillejo et al. [7]	MIBC	UC	European (Spain)	35 (GT) / 54 (GG) 5 (TT) / 54 (GG)	rs334358	9q22.33	TGFBR1	T	G	0.12 (1KG)	HR (GT/GG)=1.67 HR (TT/GG)=2.83	1.05-2.68 1.09-7.34	p-trend=0.009
MIBC Cancer-specific death	2009	Castillejo et al. [7]	MIBC	UC	European (Spain)	35 (AG) / 52 (AA) 5 (GG) / 52 (AA)	rs868	9q22.33	TGFBR1	G	A	0.12 (1KG)	HR (AG/AA)=1.85 HR (GG/AA)=3.00	1.15-2.97 1.15-7.82	p-trend=0.003
MIBC Cancer-specific death (Cystectomy-treated)	2009	Horikawa et al. [8]	MIBC	UC	Japanese	26 (Dead) / 60 (Alive)	Arg72Pro (rs1042522)	17p13.1	TP53	C	G	0.54 (1KG)	HR (CC/CG+GG)=2.76	1.11-6.84	0.028
MIBC Cancer-specific death (Radiotherapy-treated)	2014	Teo et al. [9]	MIBC (radiotherapy-treated)	Not reported	European (Denmark)	70 (Dead) / 116 (Alive)	rs1805363	11q21	MRE11	A	G	0.11 / 0.03 (1KG)	HR (A/G)=2.10	1.34–3.28	0.001 (trend)
UBC Cancer-specific death	2005	Eisenhardt et al. [10]	UBC	UC	European (Germany)	65 (CT+TT) / 15 (TT)	C825T (rs5443)	12p13.31	GNB3	T	C	0.49 (1KG)	HR (CT+TT/CC)=1.928	1.038-3.203	0.037 (log-rank)
UBC Cancer-specific death	2012	Guirado et al. [5]	UBC	UC	European (Spain)	Not reported	rs9302752	16q12.1	NOD2	A	G	0.50 (1KG)	HR (TT/CT+CC)=3.19	Not reported	0.006
Associations for overall death:															
Associations reducing the risk of overall death:															
MIBC Overall survival	2005	Leibovici et al. [2]	MIBC	Not reported	Caucasian (White)	105 (CG+CC) / 44 (GG)	174G/C (rs1800795)	7p15.3	IL6	C	G	0.14 (1KG)	HR (CG+CC/CC)=0.43	0.19-0.94	<0.05
MIBC Overall survival	2010	Chen et al. [11]	MIBC	UC	Caucasian (Northern American)	96 (Dead) / 128 (Alive) (AG/GG) 75 (Dead) / 91 (Alive) (AA/GG)	rs9906827	17q25.3	RPTOR	A	G	0.42 (1KG)	HR (AG/GG)=0.55 HR (AA/GG)=0.	0.36–0.84 0.34–0.88	0.006 0.01 0.002

						125 (Dead) / 174 (Alive) (AA+AG/GG)							54 HR (AG+AA/GG)=0.55	0.37–0.81	
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs1051013	9q32	RGS3	A/C (not reported)	T	0.84 (1KG)	HR (??/TT,)=0.44	0.20-0.95	0.0362
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs1395960	1q23.3	RGS5	A	G	0.24 (1KG)	HR (AG/GG)=0.53	0.29-0.96	0.0377
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs762861	4p16.3	RGS12	C	G	0.36 (1KG)	HR (CG/GG)=0.69	0.48-0.98	0.0389
MIBC Overall survival	2015	Zhou et al. [13]	MIBC	UC	Chinese	38 (Dead) / 118 (Alive)	rs17855750	16p12.1-p11.2	IL27	G	T	0.07 (1KG)	OR (TG+GG / TT)= 0.2 OR (TG/TT)= 0.12	0.05–0.90 0.02–0.88	0.035 0.037
NMIBC Overall survival	2014	Andrew et al. [14]	NMIBC	UC + Other	Caucasian (Northern American)	230 (Dead) / 333 (Alive), but not presented for NMIBC group	rs2662238	5q14.2	XRCC4	A	G	0.36 (1KG)	HR (GA/GG)=0.52	0.37-0.72	0.016 (log-rank)
UBC Overall survival	2007	Sanyal et al. [15]	UBC	Not reported	European (Sweden)	163 (AC+CC) / 97 (AA)	K751Q (rs13181)	19q13.3	XPD (ERCC2)	C	A	0.24 (1KG)	HR (AC+CC/AA)=0.6	0.4-0.9	0.008
UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	100 (Died) / 319 (Alive)	rs2854461	1q42.12	EPHX1	C	A	0.64 (1KG)	HR (C/A)=0.7	0.5-1.0	<0.05 and 0.02 (log-rank)
UBC Overall survival	2017	Hess et al. [17]	UBC	UC	European (Germany)	179 (Overall, death and progression	rs2279115 (c.−938C>A)	18q21.33	BCL2	A	C	0.61 / 0.39 (1KG)	HR (CC/AA)=0.24	0.07-0.83	0.024

						counts not reported)									
UBC Overall survival	2009	Mason et al. [18]	UBC	Not reported	Caucasian (Northern American)	Not reported	rs11543848	7p11.2	EGFR	A	G	0.29 (1KG)	HR (AG+AA/GG)=0.3	0.1-0.9	<0.05
UBC Overall survival	2009	Mason et al. [18]	UBC	Not reported	Caucasian (Northern American)	Not reported	rs2017000	7p11.2	EGFR	G	A	0.33 (1KG)	HR (GA+GG/AA)=0.6	0.3-1.00	<0.05
UBC Overall survival (Chemotherapy-treated)	2013	Sacerdote et al. [19]	UBC	Not reported	European (Italy)	114 (Only reported overall)	rs915927	19q13.2	XRCC1	G	A	0.32 (1KG)	HR (G/A)=0.55	0.32–0.94	0.03
UBC Overall survival (Chemotherapy-treated)	2013	Sacerdote et al. [19]	UBC	Not reported	European (Italy)	123 (Only reported overall)	rs762507	19q13.2	XRCC1	A	G	0.29 (1KG)	HR (A/G)=0.48	0.27–0.84	0.01
UBC Overall survival (Chemotherapy-treated)	2013	Sacerdote et al. [19]	UBC	Not reported	European (Italy)	120 (Only reported overall)	rs2854501	19q13.2	XRCC1	T	C	0.82 (1KG)	HR (T/C)=0.25	0.12–0.52	0.001
UBC Overall survival (Chemotherapy-treated)	2013	Sacerdote et al. [19]	UBC	Not reported	European (Italy)	205 (Only reported overall)	rs2854509	19q13.2	XRCC1	A	C	0.18 (1KG)	HR (A/C)=0.21	0.09–0.46	0.001
UBC Overall survival (Chemotherapy-treated)	2013	Sacerdote et al. [19]	UBC	Not reported	European (Italy)	122 (Only reported overall)	rs3213255	19q13.2	XRCC1	C	T	0.32 (1KG)	HR (C/T)=0.46	0.26–0.80	0.01
Associations increasing the risk of overall death:															
MIBC Overall survival	2010	Chen et al. [11]	MIBC	UC	Caucasian (Northern American)	121 (Dead) / 169 (Alive) (GG/AA) 125 (Dead) / 175 (Alive) (GG+AG/AA)	rs10515074	5q13.1	PIK3R1	G	A	0.20 (1KG)	HR (GA/AA)=1.88 HR (AG+AA/GG)=1.83	1.27–2.78 1.24–2.69	0.002 0.002

MIBC Overall survival	2010	Chen et al. [11]	MIBC	UC	Caucasian (Northern American)	109 (Dead) / 166 (Alive) (AG/GG) 68 (Dead) / 108 (Alive) (AA/GG) 125 (Dead) / 177 (Alive) (AA+AG/GG)	rs3730050	19q13.2	AKT2	A	G	0.25 (1KG)	HR (AG/GG)=1.51 HR (AA/GG)=2.99 HR (AG+AA/GG)=1.68	1.02–2.23 1.65–5.42 1.16–2.44	0.05 0.0002 0.006
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs2344673	1q23.3	RGS5	A	G	0.05 (1KG)	HR (A/G)=1.55	1.15-2.11	0.0045
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs10917690	1q23.3	RGS5	G	A	0.29 (1KG)	HR (GG/AA)=1.88	1.19-2.96	0.0066
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs1890398	1q31.2	RGS2	C	T	0.56 (1KG)	HR (CT/TT)=1.46	1.03-2.08	0.0353
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs12035879	1q23.3	RGS5	G	A	0.68 (1KG)	HR (GG/AA)=1.65	1.02-2.66	0.0387
MIBC Overall survival	2013	Lee et al. [12]	MIBC	UC	Caucasian (Northern American)	144 (Dead) / 181 (Alive)	rs10753605	1q23.3	RGS5	C	T	0.35 (1KG)	HR (CC/TT)=1.88	1.03-3.46	0.0395
MIBC Overall survival	2013	Djukic et al. [20]	MIBC	UC	European (Serbia)	62 (Died) / 27 (Alive)	rs156697	10q25.1	GSTO2	G	A	0.56 (1KG)	HR (GG/AG+AA)=3.97	1.760–8.939	0.001
MIBC Overall survival	2013	Djukic et al. [20]	MIBC	UC	European (Serbia)	62 (Died) / 27 (Alive)	rs4925	10q25.1	GSTO1	A	C	0.18 (1KG)	HR (AA/AC+CC)=2.94	1.164–7.430	0.022
MIBC Overall survival (Platinum-based chemotherapy-treated)	2016	Xu et al. [21]	Stage 4 UBC (treated with platinum-based	UC	Chinese	41 (Overall; death and progression counts not reported)	C118T (rs11615)	19q13.32	ERCC1	T	C	0.27 / 0.33 (1KG)	HR (CC / CT+TT)=1.94	1.17-3.27	0.01

			chemotherapy)												
NMIBC Overall survival	2014	Andrew et al. [14]	NMIBC	UC + Other	Caucasian (Northern American)	230 (Dead) / 333 (Alive), but not presented for NMIBC group	rs4987059	11p15.5	DRD4	A	G	0.04 (1KG)	HR (GA/GG)=1.83	1.18-2.85	0.024 (log-rank)
NMIBC Overall survival	2014	Zhou et al. [22]	NMIBC	UC	Chinese	13 (Recurrence) / 176 (No recurrence)	rs3756712	5p15.33	PDCD6	G	T	0.40 (1KG)	HR (GG/TT+GT)=5.11	1.43-18.22	0.01
UBC Overall survival	2007	Sanyal et al. [6]	UBC	Not reported	European (Sweden)	113 (Dead) / 198 (Alive)	R139W (rs4986998)	16q22.1	NQO1	T	C	0.02 (1KG)	HR (CT+TT/CC)=1.8	1.0-3.3	0.05
UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	100 (Died) / 212 (Alive)	rs6024840	20q13.2	AURKA	C	T	0.45 (1KG)	HR (C/T)=1.4	1.0-2.0	<0.05
UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	100 (Died) / 325 (Alive)	rs1042640	2q37.1	UGT1A1	C	G	0.82 (1KG)	HR (C/G)=1.4	1.0-2.0	<0.05
UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	101 (Died) / 326 (Alive)	rs1126579	2q35	IL8RB (CXCR2)	C	T	0.60 (1KG)	HR (A/G)=1.7	1.2-2.5	<0.05 and 0.003 (log-rank)
UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	100 (Died) / 319 (Alive)	rs528778	10p14	GATA3	T	C	0.14 (1KG)	HR (T/C)=1.1	0.8-1.5	<0.05 and <0.001 (log-rank)
UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	100 (Died) / 319 (Alive)	rs1800067	16p13.12	ERCC4	A	G	0.03 (1KG)	HR (A/G)=1.8	1.2-2.9	<0.05

UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	100 (Died) / 319 (Alive)	rs1994251	20q11.21	BCL2L1	C	A	0.24 (1KG)	HR (C/A)=1.5	1.1-2.1	<0.05 and 0.01 (log-rank)
UBC Overall survival	2009	Andrew et al. [16]	UBC	Not reported	Caucasian (Northern American)	171 (Dead) / 300 (Alive)	rs9282638	3q13.33	CD80	A	G	o.87 (1KG)	HR (A/G)=1.9	1.4-2.7	<0.05 and 0.008 (log-rank)
UBC Overall survival	2014	Andrew et al. [16]	UBC	UC + Other	Caucasian (Northern American)	230 (Dead) / 333 (Alive)	rs35402311	8q11.23	RB1CC1	T	C	0.02 (1KG)	HR (CT/CC)=2.29	1.54-3.41	0.001 (log-rank)
UBC Overall survival	2017	Hess et al. [17]	UBC	UC	European (Germany)	179 (Overall, death and progression counts not reported)	rs1801018 (c.21G>A)	18q21.33	BCL2	A	G	0.53 / 0.76 (1KG)	HR (AA/GG)=3.31	1.10–9.94	0.033
UBC Overall survival	2009	Mason et al. [18]	UBC	Not reported	Caucasian (Northern American)	Not reported	rs2293347	7p11.2	EGFR	T	C	0.14 (1KG)	HR (TC+TT/CC) =1.5	1.0-2.3	<0.05
UBC Overall survival (Chemotherapy-treated)	2013	Sacerdote et al. [19]	UBC	Not reported	European (Italy)	121 (Only reported overall)	rs171140	19q13.3	ERCC2	C	A	0.37 (1KG)	HR (C/A)=2.07	1.06-4.28	0.03

CI-confidence interval; EA-effect allele; EAF-effect allele frequency; MIBC-muscle-invasive bladder cancer; NMIBC-non-muscle-invasive bladder cancer; OR-odds ratio; RA-reference allele; SNP-single nucleotide polymorphism; UBC-urinary bladder cancer; UC-urothelial carcinoma; 1KG-1000 Genomes Project.

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Supplementary Table 10. Gene clusters by functional annotation for urinary bladder cancer recurrence (DAVID tool).

	Term*	Genes	Bonferroni-adjusted p-value	FDR, %
Annotation Cluster 1 Enrichment Score: 2.72	IPR024066:Regulator of G-protein signaling domain 1	RGS10, RGS16, RGS13	0.04	0.43
	domain:RGS	RGS10, RGS16, RGS13	0.12	0.93
	SM00315:RGS	RGS10, RGS16, RGS13	0.03	1.19
	IPR016137:Regulator of G protein signalling superfamily	RGS10, RGS16, RGS13	0.11	1.35
	Signal transduction inhibitor	RGS10, RGS16, RGS13	0.15	1.55
	GO:0005096~GTPase activator activity	RGS10, RGS16, RGS13	1.00	52.55
Annotation Cluster 2 Enrichment Score: 2.42	GO:0007442~hindgut morphogenesis	GLI2, GLI3, SHH	0.01	0.02
	hsa04340:Hedgehog signaling pathway	GLI2, GLI3, SHH	0.29	3.34
	GO:0042475~odontogenesis of dentin-containing tooth	GLI2, GLI3, SHH	0.85	4.38
	GO:0042733~embryonic digit morphogenesis	GLI2, GLI3, SHH	0.86	4.54
	GO:0007224~smoothened signaling pathway	GLI2, GLI3, SHH	0.95	6.76
	GO:0030324~lung development	GLI2, GLI3, SHH	0.97	8.11
	h_shhPathway:Sonic Hedgehog (Shh) Pathway	GLI2, GLI3, SHH	0.45	8.75
	hsa05217:Basal cell carcinoma	GLI2, GLI3, SHH	0.74	12.39
	GO:0007411~axon guidance	GLI2, GLI3, SHH	1.00	29.44
	GO:0007507~heart development	GLI2, GLI3, SHH	1.00	36.49

* As listed in DAVID
FDR-false discovery rate

491 Supplementary Table 11. Enrichment in functional pathways for genes reported for bladder
492 cancer recurrence (DAVID tool).

Term*	Genes list	Bonferroni-adjusted p value	FDR, %
hsa05200:Pathways in cancer	CXCL8, NFKBIA, IGF1, CDH1, BIRC5, GLI2, GLI3, MMP2, SHH	0.001	0.01
GO:0007442~hindgut morphogenesis	GLI2, GLI3, SHH	0.008	0.02
GO:0045944~positive regulation of transcription from RNA polymerase II promoter	VDR, SLC11A1, IL17A, IFNG, NFKBIA, IGF1, GLI2, GLI3, SHH	0.04	0.09
GO:0048566~embryonic digestive tract development	CXCL8, GLI2, GLI3	0.15	0.37
IPR024066:Regulator of G-protein signaling domain 1	RGS10, RGS16, RGS13	0.04	0.43
GO:0043066~negative regulation of apoptotic process	NFKBIA, IGF1, BIRC5, GLI2, GLI3, SHH	0.26	0.72
domain:RGS	RGS10, RGS16, RGS13	0.12	0.93
GO:0000060~protein import into nucleus translocation	SLC11A1, IFNG, NFKBIA	0.39	1.16
sequence variant	ICAM1, CWC27, NEIL2, NFKBIA, IGF1, CDH1, BIRC5, SOD1, RGS16, GLI2, GLI3, MMP2, SHH, RGS13, GSS, DROSHA, SLC11A1, RGS10, VDR, ERCC6, GPX4, IFNG, ALDH2, DDX20	0.13	1.01
mutagenesis site	DROSHA, VDR, GPX4, NEIL2, NFKBIA, CDH1, BIRC5, RGS16, SOD1, SHH	0.13	1.05
IPR016137:Regulator of G protein signalling superfamily	RGS10, RGS16, RGS13	0.11	1.35
Signal transduction inhibitor	RGS10, RGS16, RGS14	0.15	1.55
SM00315:RGS	RGS10, RGS16, RGS15	0.03	1.19
GO:0005615~extracellular space	ICAM1, IL17A, IFNG, CXCL8, IGF1, SOD1, MMP2, SHH	0.15	1.90
Disease mutation	GSS, VDR, ERCC6, NFKBIA, CDH1, GLI2, SOD1, GLI3, MMP2, SHH	0.23	2.45
hsa05323:Rheumatoid arthritis	ICAM1, IL17A, IFNG, CXCL8	0.23	2.56
hsa04340:Hedgehog signaling pathway	GLI2, GLI3, SHH	0.29	3.34
GO:0042475~odontogenesis of dentin-containing tooth	GLI2, GLI3, SHH	0.85	4.38
GO:0042733~embryonic digit morphogenesis	GLI2, GLI3, SHH	0.86	4.54
h_freePathway:Free Radical Induced Apoptosis	GSS, CXCL8, SOD1	0.21	3.47

*As listed in DAVID.
FDR-false discovery rate

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494 Supplementary Table 12. Enrichment in functional pathways for genes reported for bladder
495 cancer death (DAVID tool).

Term*	Genes list	Bonferroni-adjusted p value	FDR, %
hsa05212:Pancreatic cancer	TGFBR1, BCL2L1, PIK3R1, AKT2	0.05	0.47
GO:0046326~positive regulation of glucose import	PIK3R1, TERT, AKT2	0.22	0.74
Ubl conjugation	XRCC4, RGS3, TGFBR1, DRD4, AURKA, PIK3R1, TERT, AKT2	0.06	0.61
hsa05220:Chronic myeloid leukemia	TGFBR1, BCL2L1, PIK3R1, AKT2	0.06	0.64
GO:0005829~cytosol	XRCC4, RGS3, RB1CC1, AURKA, GSTO2, GNB3, BCL2L1, PIK3R1, RPTOR, AKT2, MRE11	0.06	0.79
GO:0007165~signal transduction	RGS12, TGFBR1, GATA3, CXCR2, GNB3, PIK3R1, AKT2	0.47	1.89
hsa05166:HTLV-I infection	TGFBR1, BCL2L1, PIK3R1, TERT, AKT2	0.24	2.63
Phosphoprotein	XRCC4, TGFBR1, CXCR2, AURKA, BCL2L1, RPTOR, MRE11, RGS12, CD80, RGS3, GATA3, RB1CC1, TERT, PIK3R1, AKT2	0.29	3.45
Transferase	TGFBR1, AURKA, GSTO2, UGT1A1, PIK3R1, TERT, AKT2	0.31	3.78
GO:0005515~protein binding	XRCC4, TGFBR1, DRD4, CXCR2, AURKA, BCL2L1, RPTOR, MRE11, CD80, RGS3, GATA3, RB1CC1, GSTO2, GNB3, TERT, PIK3R1, AKT2	0.37	4.23

*As listed in DAVID
FDR-false discovery rate.

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