

MasterClass in Bladder Cancer 2026

June 9th

**Centro de Formación
y Simulación Avanzada,**
Hospital Universitario 12 de Octubre
Avda. de Córdoba, s/n. Madrid

Scientific coordinators:

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Medical Oncology Department,
Hospital Universitario 12 de Octubre, Madrid

Dr. Félix Guerrero
Urology Department,
Hospital Universitario 12 de Octubre, Madrid



BCG monotherapy is here to stay

Dr. José Luis Domínguez Escrig,
Servicio de Urología. Fundación I.V.O., Valencia.
Servicio de Urología. Hospital ASCIRES, Valencia.



Trial Participation

- Combat BRS
- Presurgy
- Arquer
- STORZ
- Angiodynamics
- IPSEN
- Pfizer
- Janssen



José L. Domínguez Escrig LMS. MD. DM. MRCS(Eng). FRCS(Urol).

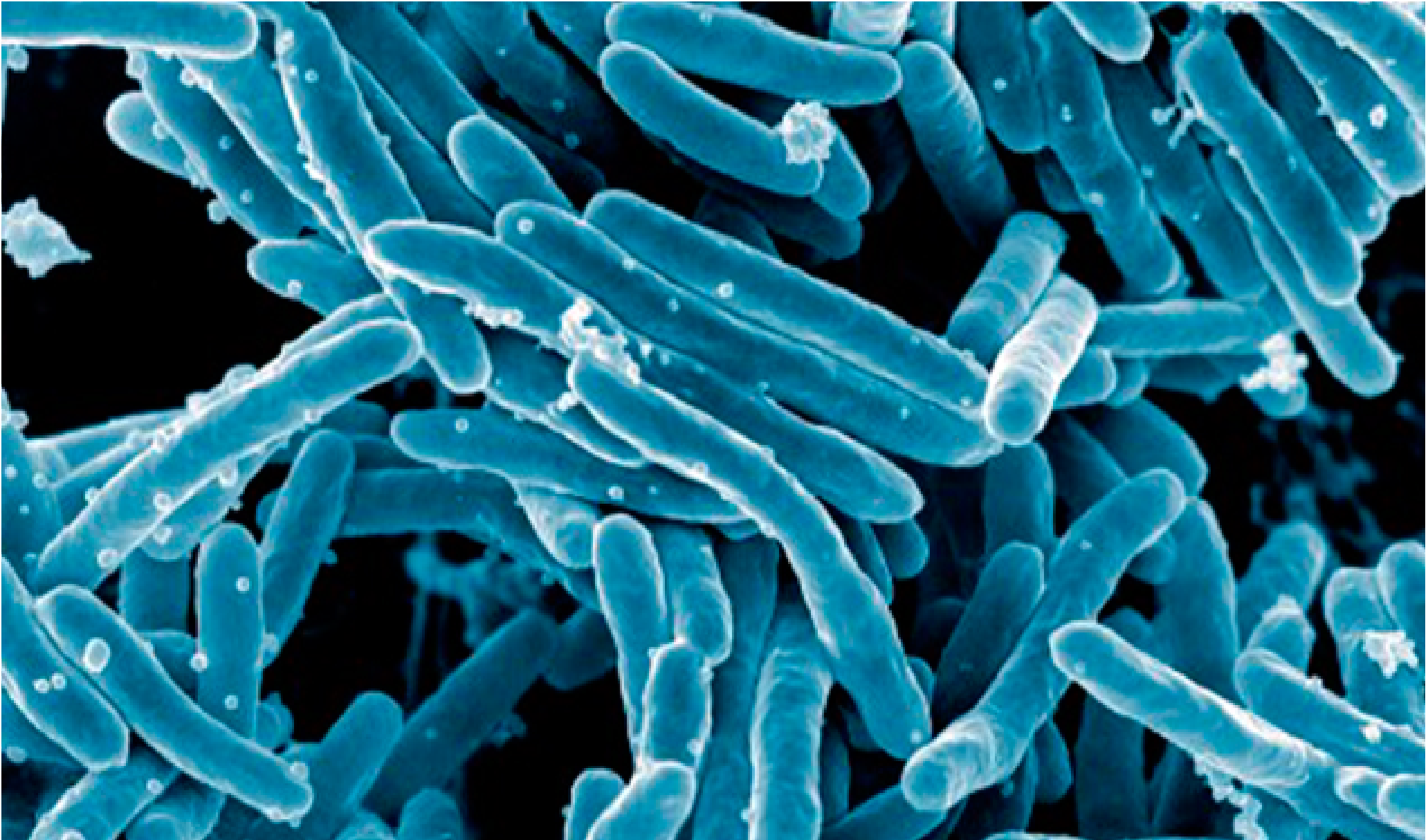
Trial Design

- Presurgy-Physion
- Arquer

Jefe Clínico Servicio de Urología
Fundación Instituto Valenciano de Oncología (I.V.O.).

Jefe de Urología
Hospital Biomédico ASCIRES

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INTRACAVITARY BACILLUS CALMETTE-GUERIN IN THE TREATMENT OF SUPERFICIAL BLADDER TUMORS

A. MORALES,* D. EIDINGER AND A. W. BRUCE

From the Departments of Urology, and Microbiology and Immunology, Queen's University, Kingston, Ontario, Canada

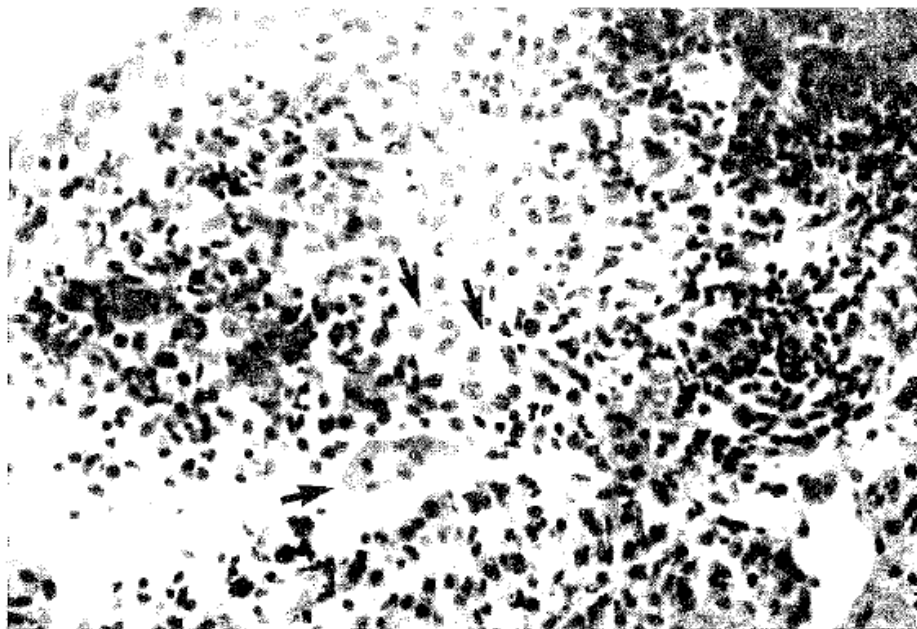


FIG. 2. Granulomatous reaction seen in biopsy of bladder. Arrows indicate giant cells.

TABLE 1. *Effect of BCG on the rate of tumor recurrence*

Pt.*	Calendar of Cystoscopic Examinations				
	Pre-BCG		Post-BCG		
1	May 74 Pos.† (2)‡	Aug. 74 Pos. (2)	Jan. 75 Pos. (1)	May 75 Neg.§	Aug. 75 Neg.
2	Jan. 73 Pos. (1)	June 73 Pos. (1)	Oct. 73 Pos. (1)	Jan. 74 Pos. (1)	Mar. 74 Died
3	Sept. 73 Pos. (2)	Feb. 74 Pos. (1)	Sept. 74 Pos. (2)	Jan. 75 Neg.	Apr. 75 Neg.
4	July 74 Pos. (1)	Sept. 74 Pos. (1)	Jan. 75 Pos. (1)	Apr. 75 Neg.	June 75 Neg.
5	July 74 Pos. (1)	Nov. 74 Neg.	Jan. 75 Pos. (4)	May 75 Neg.	July 75 Neg.
6	Sept. 73 Pos. (1)	Feb. 74 Neg.	Aug. 74 Pos. (3)	June 75 Neg.	Aug. 75 Neg.
7	Feb. 73 Pos. (3)	June 73 Pos. (2)	Sept. 73 Pos. (1)	Nov. 74 Neg.	May 75 Neg.

* Two patients with insufficient followup are omitted.

† Cystoscopy positive for tumor recurrence.

‡ Numbers in parentheses indicate number of recurrences in each examination.

§ Cystoscopy negative for tumor recurrence.



... Impact on recurrence

A systematic review of intravesical bacillus Calmette-Guérin plus transurethral resection vs transurethral resection alone in Ta and T1 bladder cancer

M.D. SHELLEY, H. KYNASTON*, J. COURT, T.J. WILT†, B. COLES, K. BURGON and M.D. MASON



Table 2 Log hazard ratios and variances for the included trials. A subgroup meta-analysis was undertaken on group 1 (medium/high-risk patients) and group 2 (possibility of low-risk patients included in the study). The weighted mean ln(hr) was for the combined meta-analysis

			Proportion recurred at 1 year	
Trial	Log hazard ratio ((TUR + BCG)/TUR)	Variance	TUR	TUR + BCG
Medium/high-risk patients				
[12]	−0.482	0.058	43/116	28/98
[13]	−0.613	0.462	4/6	3/6
[14]	−1.740	0.150	31/39	6/43
[15]	−0.742	0.049	39/43	27/41
Subgroup meta-analysis				
	−0.783	0.022		
Medium/high risk but unclear if low risk included				
[16]	−0.818	0.099	14/33	11/67
[17]	−1.520	0.323	13/20	4/20
Subgroup meta-analysis				
	−0.983	0.076		
Overall meta-analysis: weighted mean ln(hr)				
	−0.827	0.017		

Table 3 The Peto odds ratio for the number of patients with disease recurrence at 12 months for the six trials. A subgroup meta-analysis was conducted on the medium/high-risk patients and those with a possibility of low-risk patients included in the study. A Peto odds ratio of >1 favours TUR and of <1 favours BCG + TUR

Study/ group	BCG + TUR, n/N	TUR, n/N	Weight, %	Peto odds ratio (99% CI)
Medium/high-risk patients				
[12]	28/98	43/116	42.2	0.68 (0.32–1.44)
[13]	3/6	4/6	2.8	0.53 (0.03–9.58)
[14]	6/43	31/39	18.3	0.07 (0.02–0.23)
[15]	27/41	39/43	12.8	0.23 (0.06–0.91)
Subtotal	64/188	117/204	76.1	0.33 (0.19–0.58)
Medium/high, possibly some low-risk patients				
[16]	11/67	14/33	14.9	0.25 (0.07–0.89)
[17]	4/20	13/20	8.9	0.17 (0.03–0.85)
Subtotal	15/87	27/53	23.9	0.22 (0.08–0.59)
Total	79/275	144/257	100.0	0.30 (0.18–0.49)

INTRAVESICAL BACILLUS CALMETTE-GUERIN VERSUS MITOMYCIN C FOR SUPERFICIAL BLADDER CANCER: A FORMAL META-ANALYSIS OF COMPARATIVE STUDIES ON RECURRENCE AND TOXICITY

A. BÖHLE,* D. JOCHAM* AND P. R. BOCK*

From the Department of Urology, Medical University of Lübeck, Lübeck, Germany, and IFAG Basel AG, Institute for Medical Research and Biostatistics, Basel, Switzerland



TABLE 1. *Characteristics of studies*

References	No. Evaluable Pts.	BCG Maintenance (1 or more yrs.)	Study Quality*	Predominant Risk Group ³
Ayed et al ²¹	270	Yes	B	Intermediate
Debruyne et al ¹⁰	325	No	A	Intermediate
Jauhiainen et al ²²	91	Yes	A	High
Krege et al ²³	214	No	A	Intermediate
Lamm et al ¹²	363	Yes	A	High
Lundholm et al ¹³	250	Yes	A	High
Millán-Rodríguez et al ⁹	464	Yes	B	Intermediate
Nogueira et al ²⁴	210	No	A	Intermediate
Pagano et al ²⁵	114	Yes	B	Intermediate
Vegt et al ¹¹	387	No	A	Intermediate
Lee et al ²⁶	61	No	B	High

* Adapted from original definition of Cochrane Reviews as A—prospective, randomized, controlled clinical trials and B—observational cohort studies or prospective, controlled clinical trials with missing randomization information.⁵

11 eligible clinical trials

n=1,421 BCG-treated and 1,328-MMC treated patients

Recurrence rate BCG-treated = 38.6% vs 46.4% in MMC-treated group

An overall statistically significant superiority of BCG versus mitomycin C efficacy in reducing tumor recurrence was detected (OR 0.56, 95% CI 0.38 to 0.84, p= 0.005).

In the subgroup treated with BCG maintenance all 6 individual studies showed a significant superiority of BCG over MMC (OR 0.43, 95% CI 0.35 to 0.53, p<0.001).

INTRAVESICAL BACILLUS CALMETTE-GUERIN VERSUS MITOMYCIN C FOR SUPERFICIAL BLADDER CANCER: A FORMAL META-ANALYSIS OF COMPARATIVE STUDIES ON RECURRENCE AND TOXICITY

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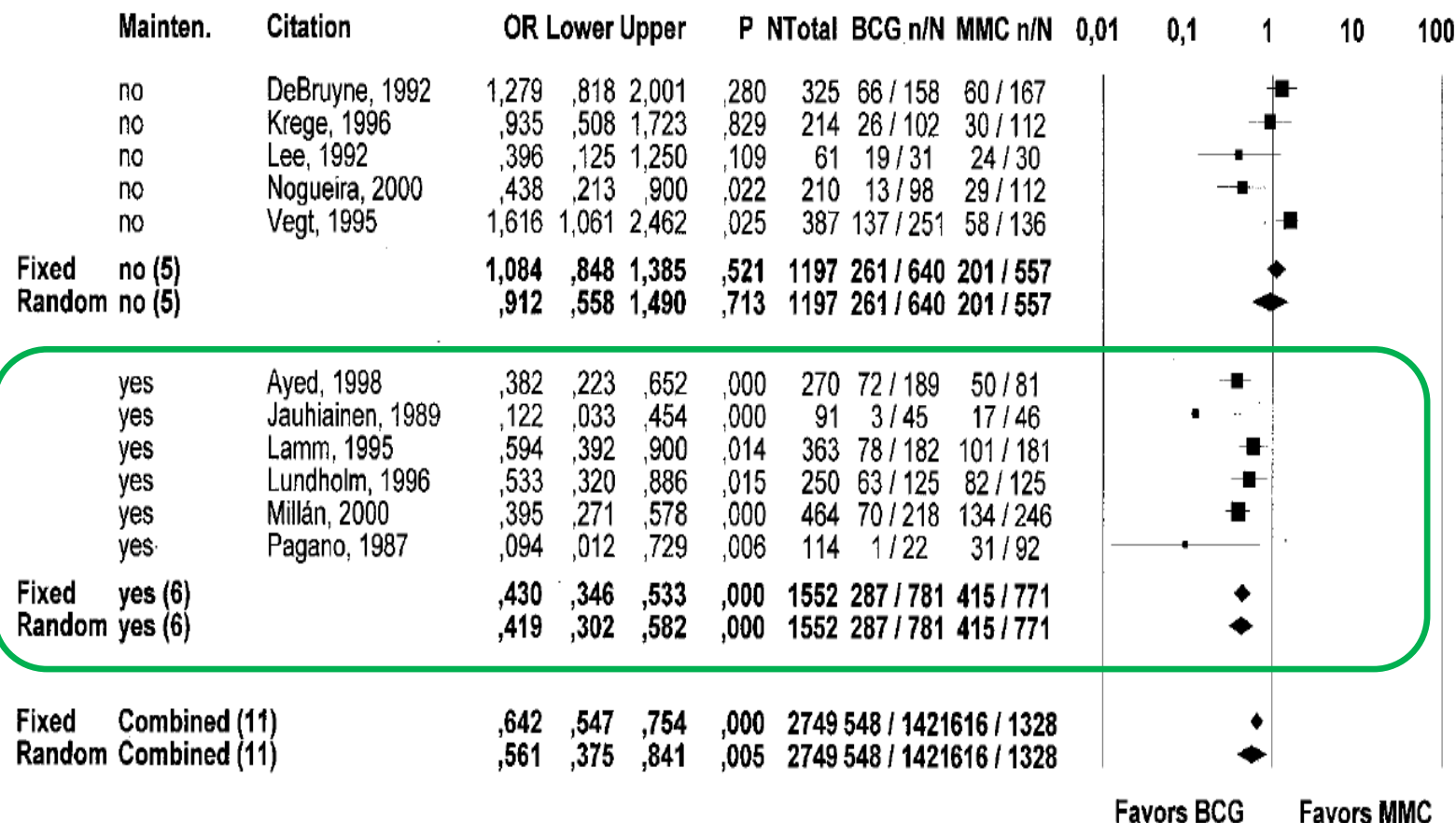
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Tumor recurrence (all studies by maintenance) with OR as effect size. *Mainten.*, BCG maintenance regimen

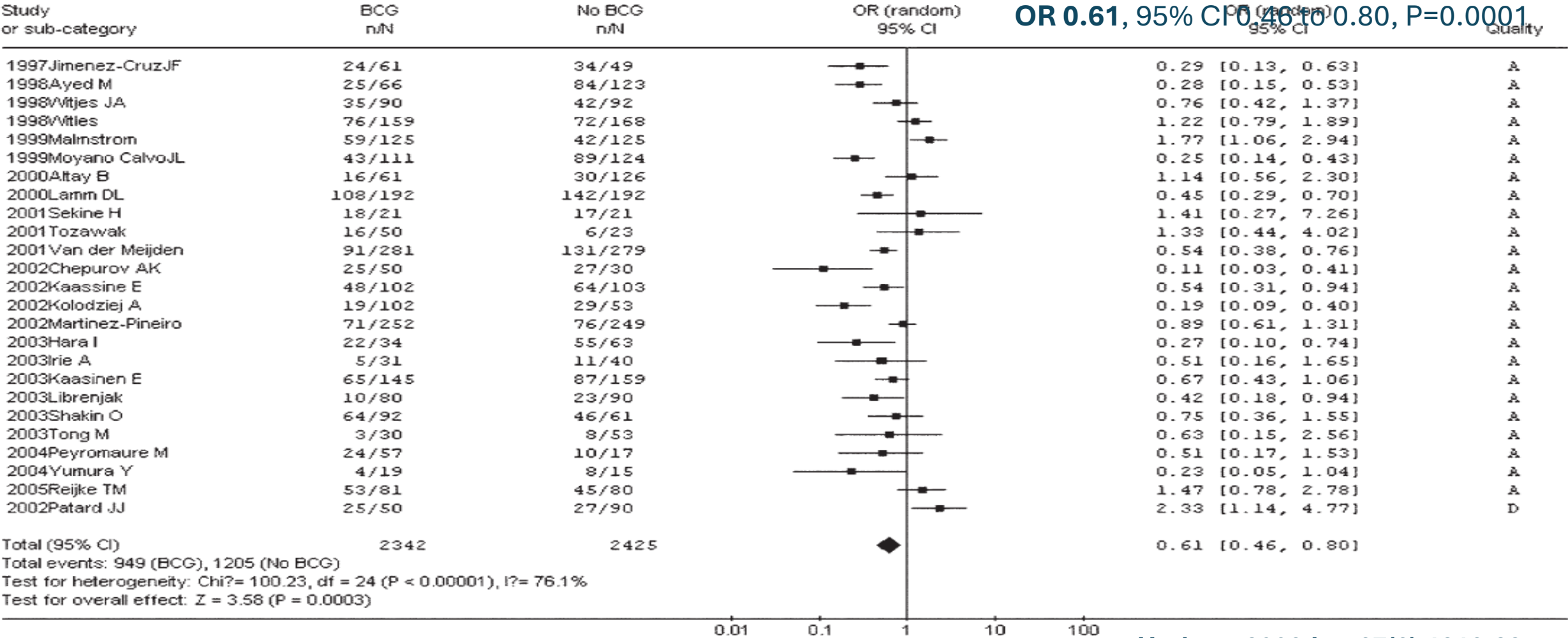
CAN INTRAVESICAL BACILLUS CALMETTE-GUÉRIN REDUCE RECURRENCE IN PATIENTS WITH SUPERFICIAL BLADDER CANCER? A META-ANALYSIS OF RANDOMIZED TRIALS

RUI FA HAN AND JIAN GANG PAN



25 trials n= 4767 patients.
Recurrence BCG 40.5% vs. 49.7% non-

BCG





An Individual Patient Data Meta-Analysis of the Long-Term Outcome of Randomised Studies Comparing Intravesical Mitomycin C versus Bacillus Calmette-Guérin for Non-Muscle-Invasive Bladder Cancer

Per-Uno Malmström^{a,*}, Richard J. Sylvester^b, David E. Crawford^c, Martin Friedrich^d, Susanne Krege^e, Erkki Rintala^f, Eduardo Solsona^g, Savino M. Di Stasi^h, J. Alfred Witjesⁱ



9 Trials
n= 2820
Follow-up 4.4 yr
43% recurred.

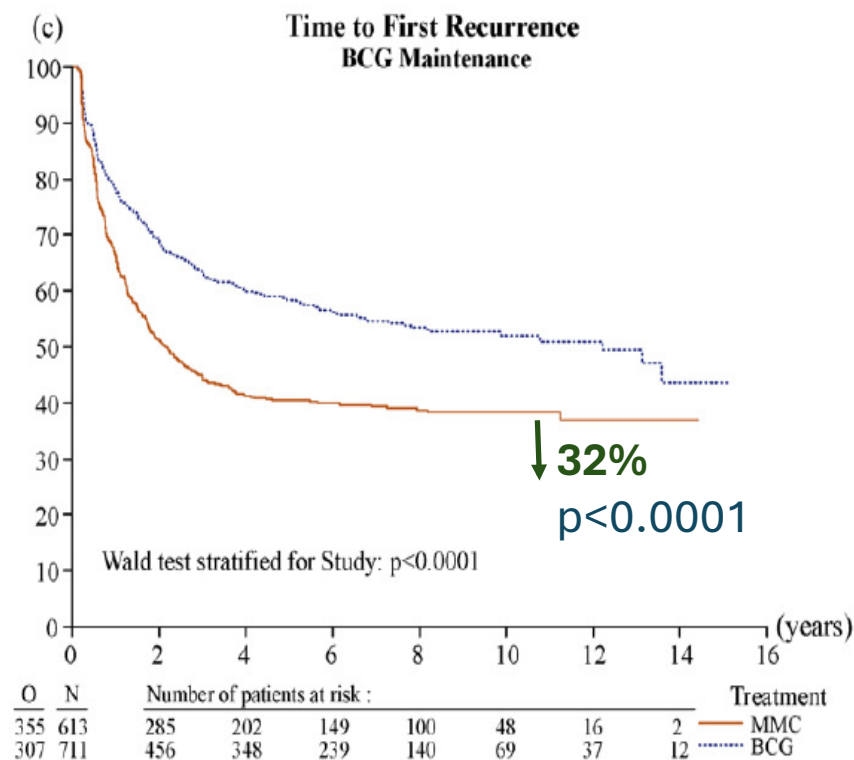
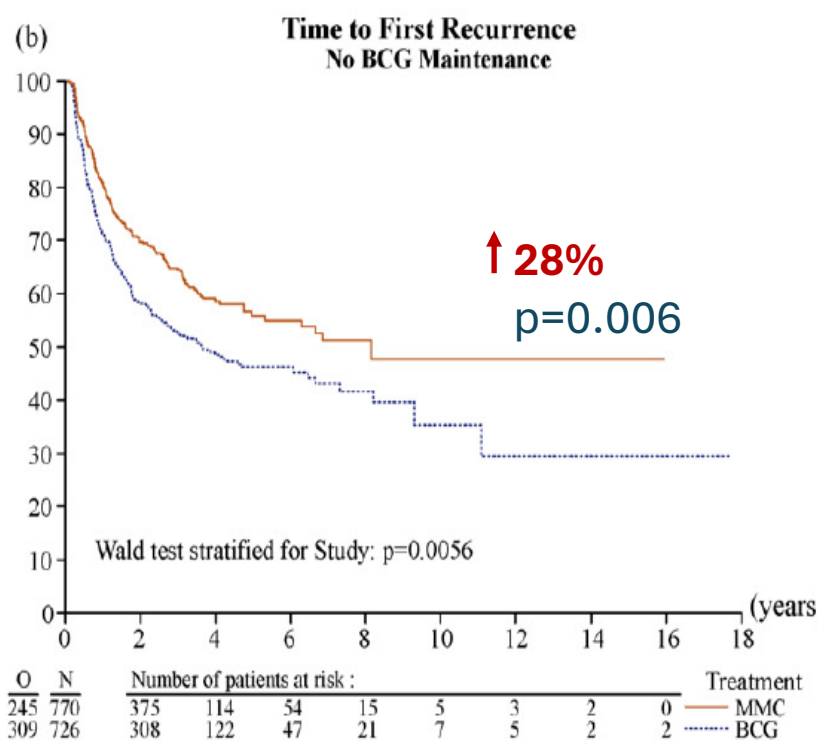
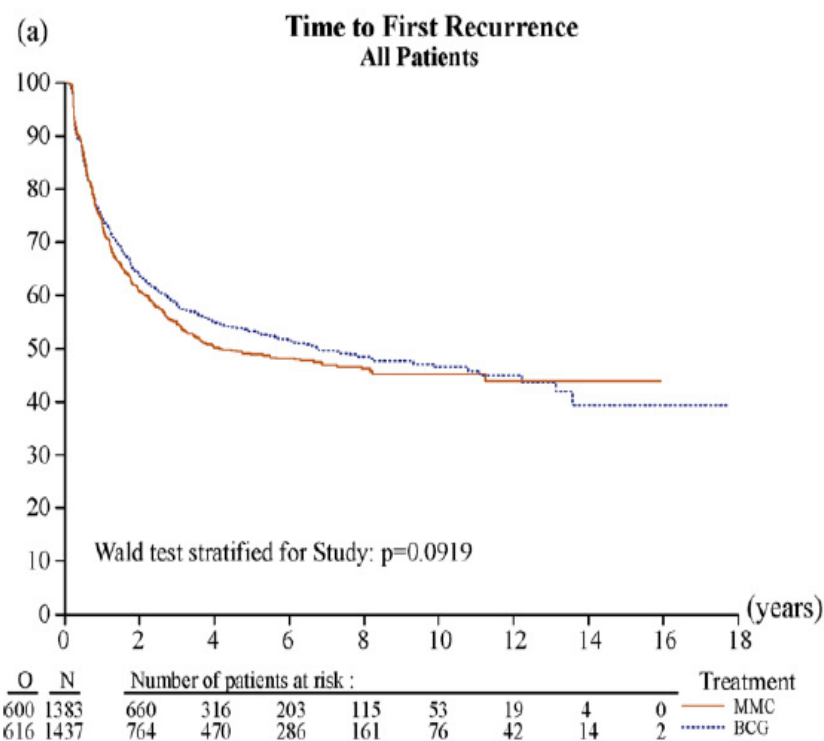
Reference	BCG strain/dosage	MMC dosage	Treatment duration	Prior chemo allowed	Comments
Rintala et al [13]	Pasteur F	20–40 mg	Both: 6 w + 24 m	Yes	BCG intermediate dose; 91 patients
Witjes et al [14]	RIVM	30 mg	MMC: 4 w + 5 m BCG: 1–2 × 6 w	No	349 patients
Witjes et al [15]	Tice and RIVM	30 mg	MMC: 4 w + 5 m BCG: 1–2 × 6 w	No	437 patients
Lamm et al [11]	Tice	20 mg	Both: 6 w + 12 m	Yes	445 patients
Krege et al [10]	Connaught	20 mg	MMC: 12 bim + 12 m BCG: 6 w + 4 m	Yes	215 patients
Malmström et al [12]	Pasteur D	40 mg	Both: 6 w + 10 m + 4 q	Yes	250 patients
Ojea et al [17]	Connaught	30 mg	Both: 6 w + fortnightly × 6	Yes	BCG 1/3 and 1/6 dose; 430 patients
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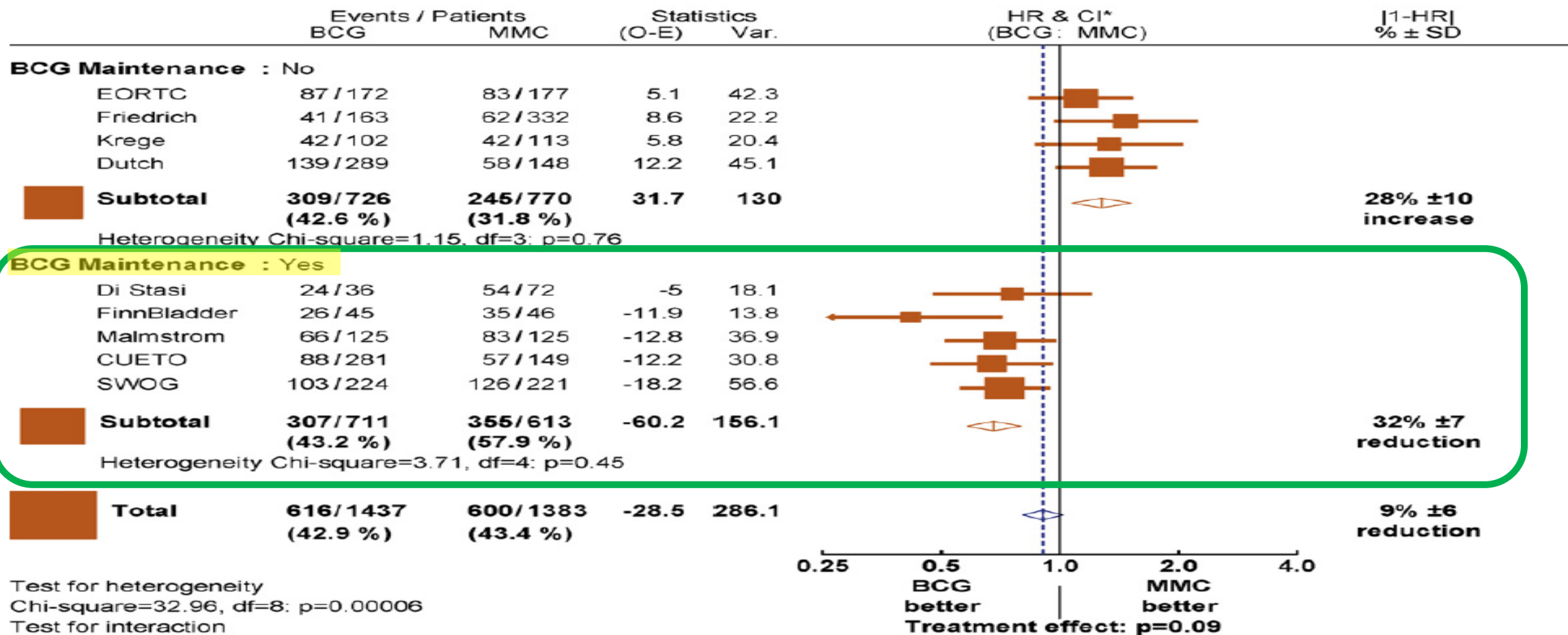
Overall, there was no difference in the time to first recurrence (p = 0.09) between BCG and MMC. With BCG maintenance, a 32% reduction in risk of recurrence on BCG compared to MMC was found (p<0.0001), Without BCG maintenance, a 28% risk increase (p = 0.006) for BCG compared to MMC.



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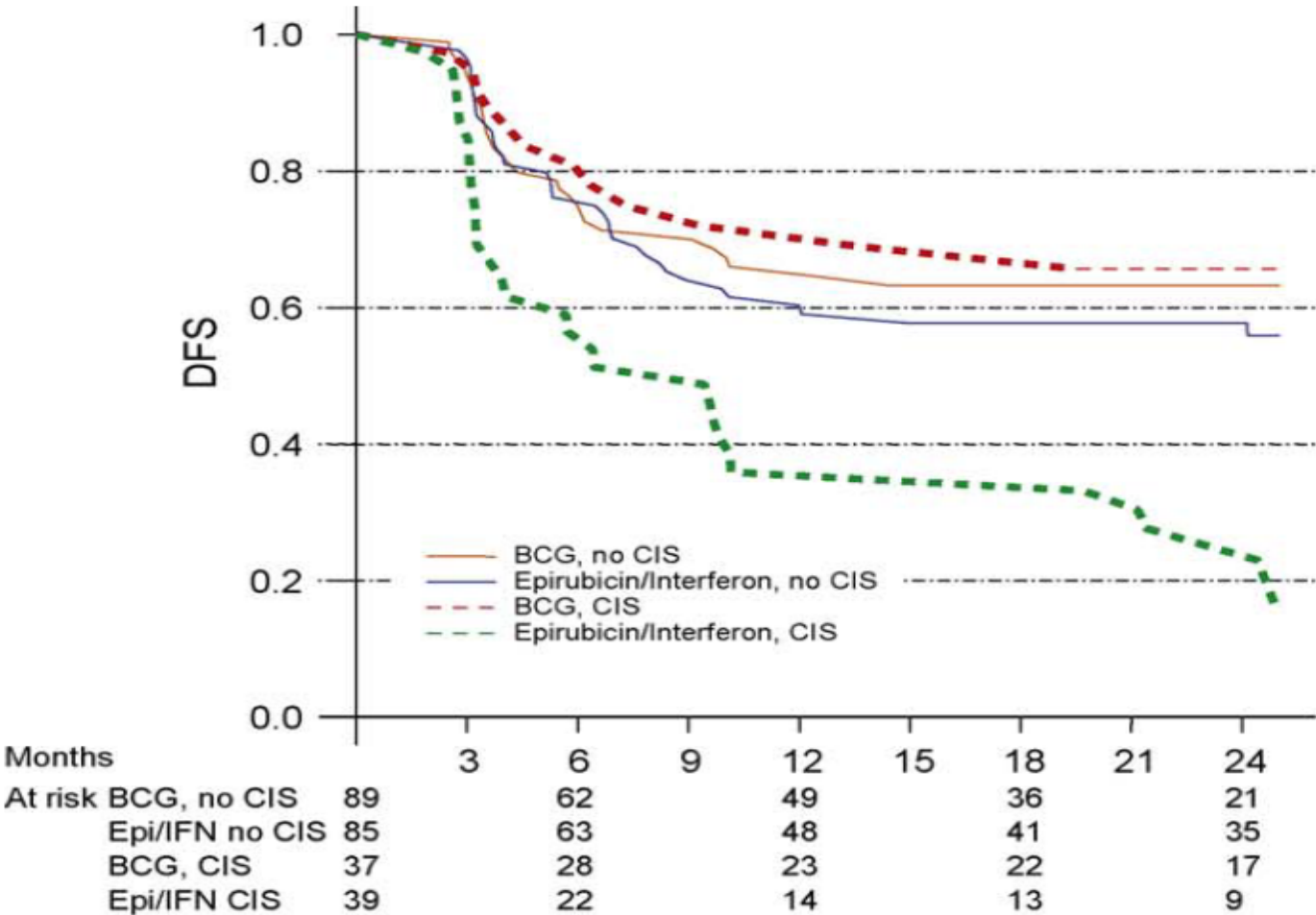
Time to First Recurrence





Bacillus Calmette-Guérin Is Superior to a Combination of Epirubicin and Interferon- α 2b in the Intravesical Treatment of Patients with Stage T1 Urinary Bladder Cancer. A Prospective, Randomized, Nordic Study

Miloš Duchek^a, Robert Johansson^b, Staffan Jahnson^c, Oddvar Mestad^d, Pekka Hellström^e, Sverker Hellsten^f, Per-Uno Malmström^{g,*}
 Members of the Urothelial Cancer Group of the Nordic Association of Urology



RCT n=250

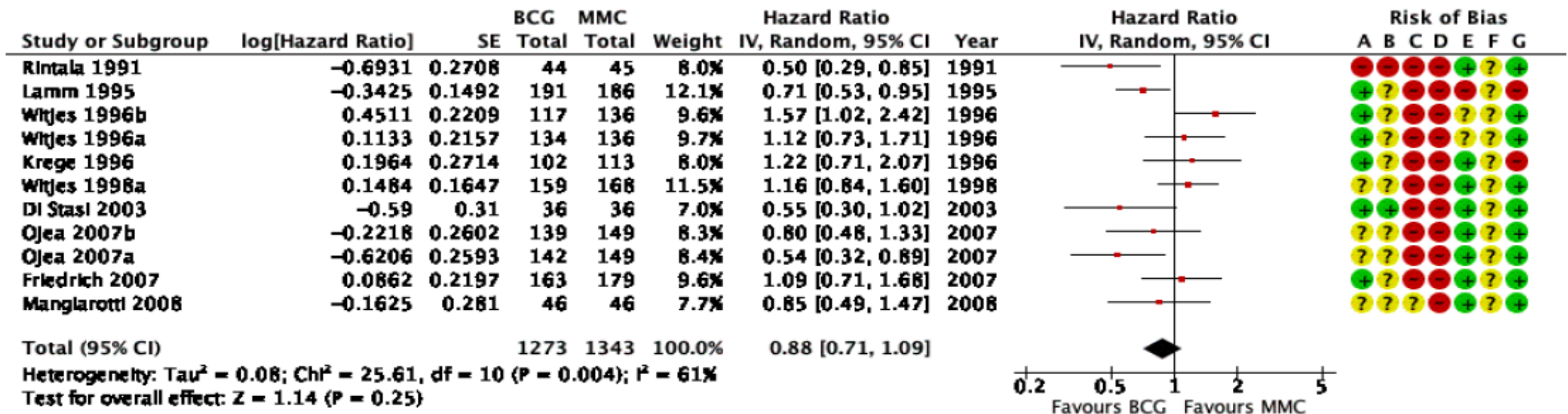
DFS
 62% in Epi+Inta2b vs. 73% in BCG (p= 0.065)

At 24 mo:
 Significant difference in favour of BCG (p=0.012) regarding recurrence.

No diff. in terms of progression.

Superiority of BCG mainly in those with concomitant CIS.

Figure 6. Forest plot of comparison: 1 Bacillus Calmette-Guérin (BCG) versus mitomycin C (MMC), outcome: 1.3 Time to recurrence.



Time to recurrence: BCG may reduce the time to recurrence compared to MMC (HR 0.88, 95% CI 0.71 to 1.09; participants = 2616, studies= 11, 1273 participants in the BCG arm and 1343 in the MMC arm; low-certainty evidence). This corresponds to 41 fewer recurrences (104 fewer to 29 more) with BCG at five years.



...Impact on progression

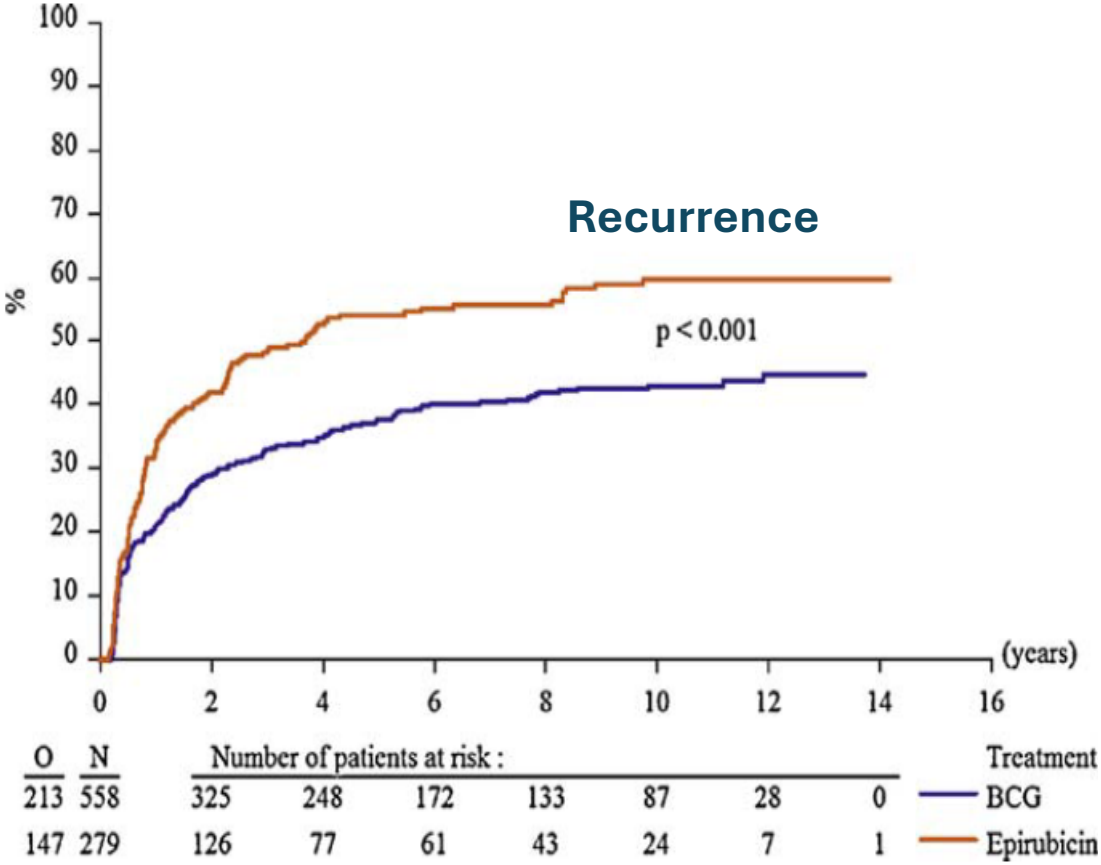


Long-Term Efficacy Results of EORTC Genito-Urinary Group Randomized Phase 3 Study 30911 Comparing Intravesical Instillations of Epirubicin, Bacillus Calmette-Guérin, and Bacillus Calmette-Guérin plus Isoniazid in Patients with Intermediate- and High-Risk Stage Ta T1 Urothelial Carcinoma of the Bladder

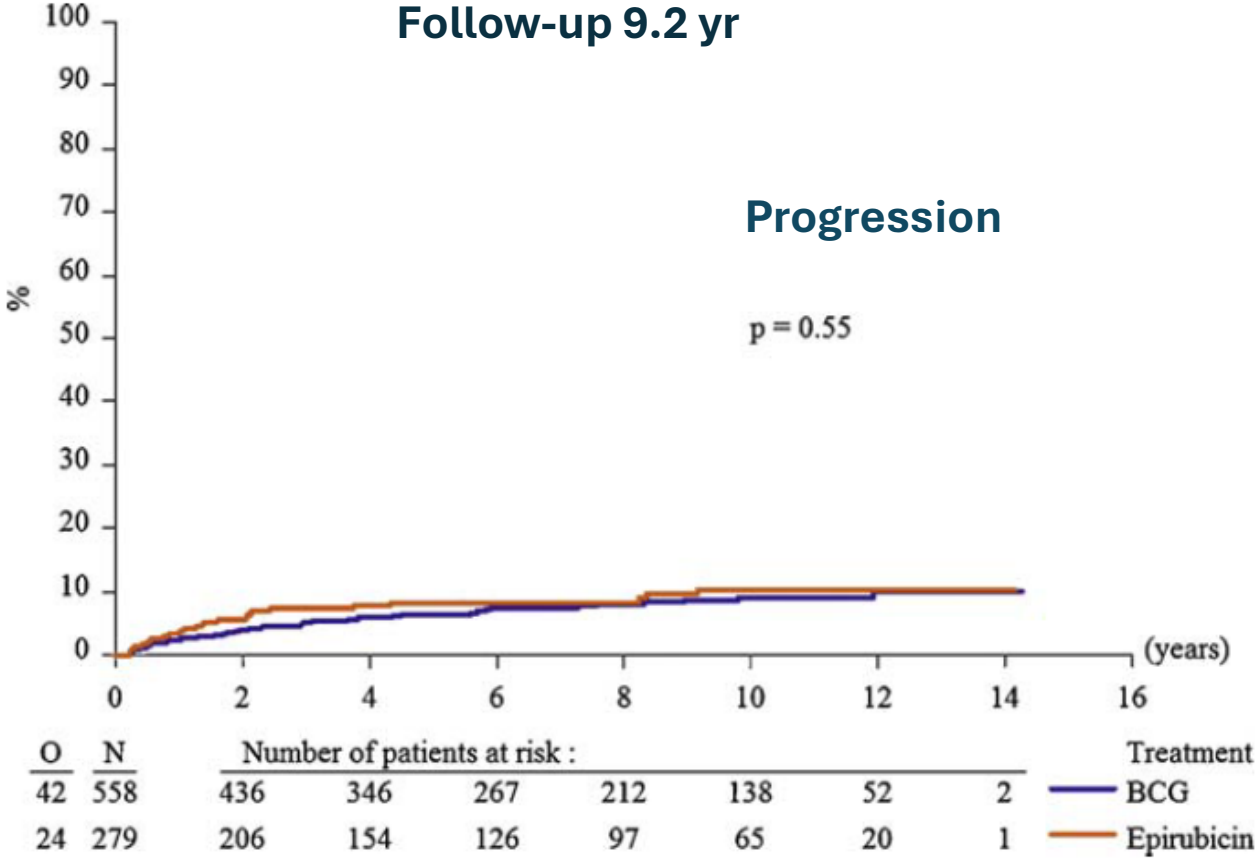
Richard J. Sylvester^{a,*}, Maurizio A. Brausi^b, Wim J. Kirkels^c, Wolfgang Hoeltl^d, Fernando Calais Da Silva^e, Philip H. Powell^f, Stephen Prescott^g, Ziya Kirkali^h, Cees van de Beekⁱ, Thierry Gorlia^a, Theo M. de Reijke^j
 EORTC Genito-Urinary Tract Cancer Group



RCT
 n= 837 323 HR + 497 IR
 Follow-up 9.2 yr



Cumulative incidence of first recurrence. BCG = bacillus Calmette-Guérin. O = observed number of events; N = number of patients.



Cumulative incidence of progression. BCG = bacillus Calmette-Guérin. O = observed number of events; N = number of patients.

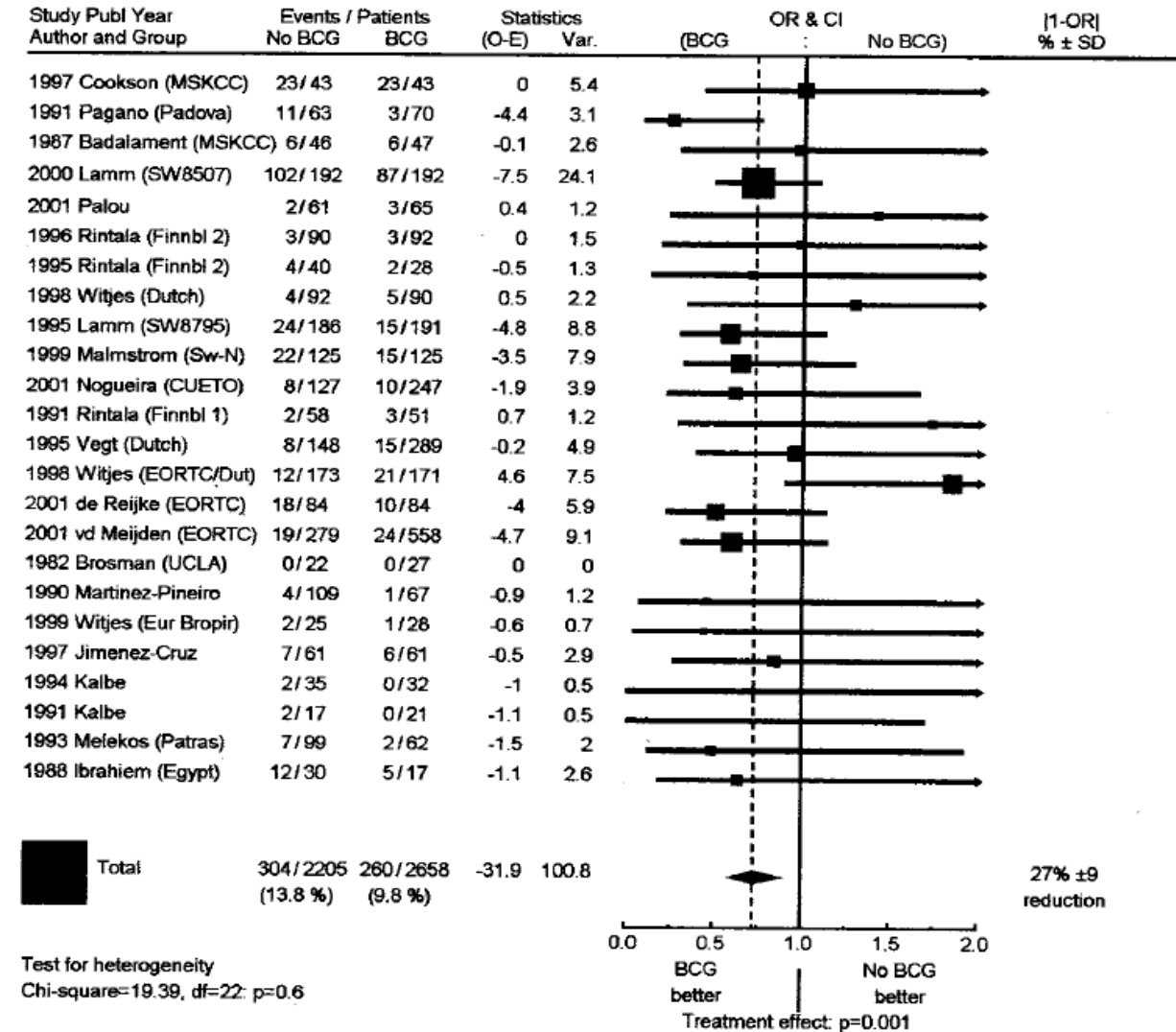
INTRAVESICAL BACILLUS CALMETTE-GUERIN REDUCES THE RISK OF PROGRESSION IN PATIENTS WITH SUPERFICIAL BLADDER CANCER: A META-ANALYSIS OF THE PUBLISHED RESULTS OF RANDOMIZED CLINICAL TRIALS

RICHARD J. SYLVESTER, ADRIAN P. M. VAN DER MEIJDEN AND DONALD L. LAMM*

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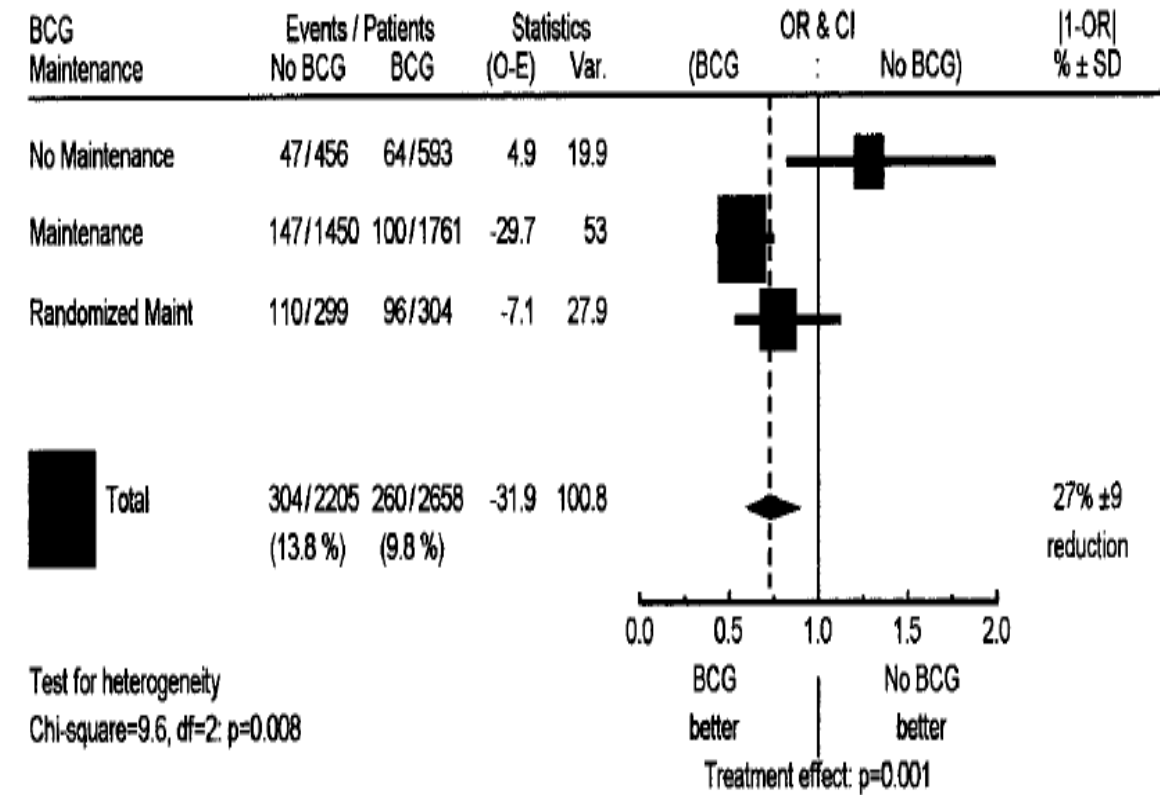
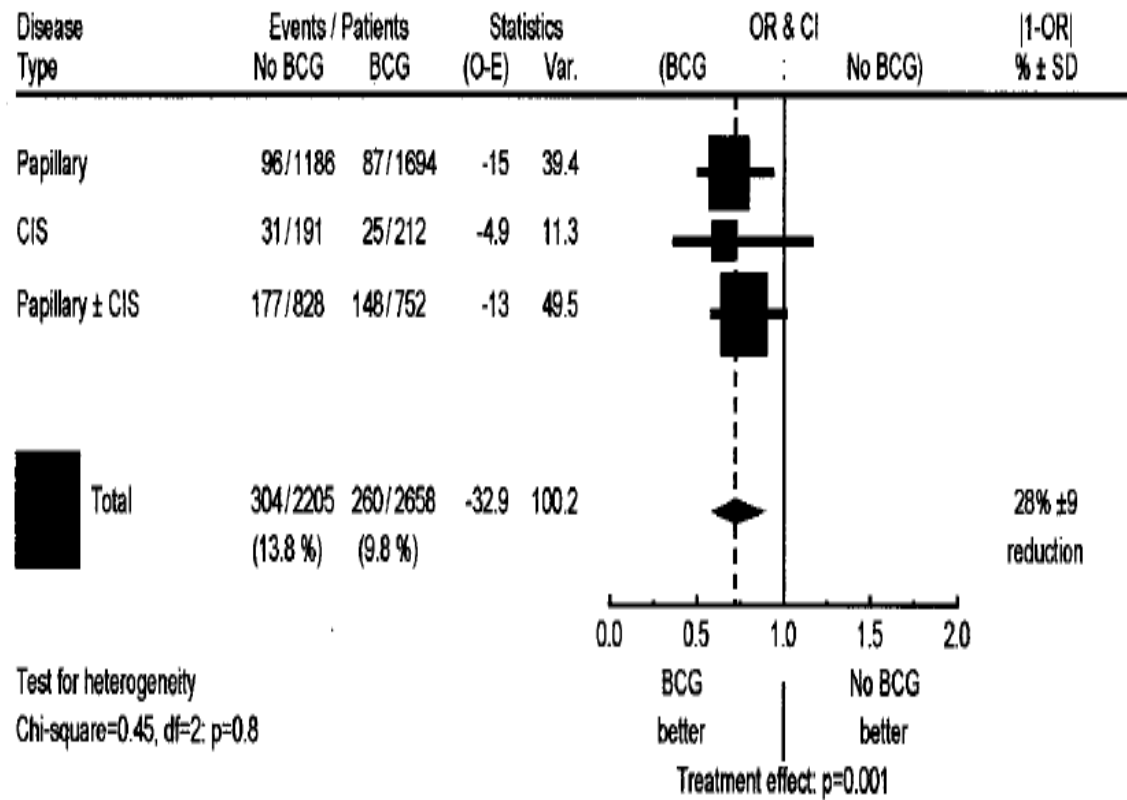
	No. Pts. (%)
Randomized	5,456
Evaluable:	4,863 (89.1)
No BCG	2,205 (45.3)
BCG	2,658 (54.7)
Disease type:	
Papillary	3,967 (81.6)
Primary or concomitant Ca in situ	896 (18.4)
T category and grade (6 papillary only trials):	1,622
Ta	682 (49.9)
T1	684 (50.1)
Tx	256
G1	533 (37.5)
G2	779 (54.9)
G3	108 (7.6)
Gx	202
Treatment comparison:	
BCG vs. transurethral resection only ^{5,6}	219 (4.5)
BCG maintenance vs. no maintenance ⁷⁻⁹	603 (12.4)
BCG + mitomycin C vs. mitomycin C ¹⁰⁻¹²	432 (8.9)
BCG vs. mitomycin C ¹³⁻¹⁸	1,891 (38.9)
BCG vs. epirubicin ^{20,22}	1,005 (20.7)
BCG vs. transurethral resection only or epirubicin ¹⁹	161 (3.3)
BCG vs. thiotepa ²³	49 (1.0)
BCG vs. doxorubicin or thiotepa ²¹	176 (3.6)
BCG vs. interferon α ^{25,26}	189 (3.9)
BCG vs. bropirimine ²⁴	53 (1.1)
BCG vs. keyhole limpet hemocyanin ²⁷	38 (0.8)
BCG vs. transurethral resection only or maltose tetrapalmitate ²⁸	47 (1.0)
BCG maintenance:	
No maintenance ^{5,12,17,18}	593 (22.3)
Maintenance ^{6-11,13-16,19-28}	2,065 (77.7)
BCG strain:	
Tice ^{12,13,17,22-24}	1,034 (38.9)
Connaught ^{8,9,15,20,26,27}	641 (24.1)
Pasteur ^{6,7,10,11,14,16,19,21,25}	603 (22.7)
RIVM ^{17,18}	320 (12.0)
A. Frappier ^{5,28}	60 (2.3)



INTRAVESICAL BACILLUS CALMETTE-GUERIN REDUCES THE RISK OF PROGRESSION IN PATIENTS WITH SUPERFICIAL BLADDER CANCER: A META-ANALYSIS OF THE PUBLISHED RESULTS OF RANDOMIZED CLINICAL TRIALS

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BCG = bacillus Calmette-Guérin; bim = bimonthly; CIS = carcinoma in situ; m = monthly; MMC = mitomycin C; q = quarterly; w = weekly.



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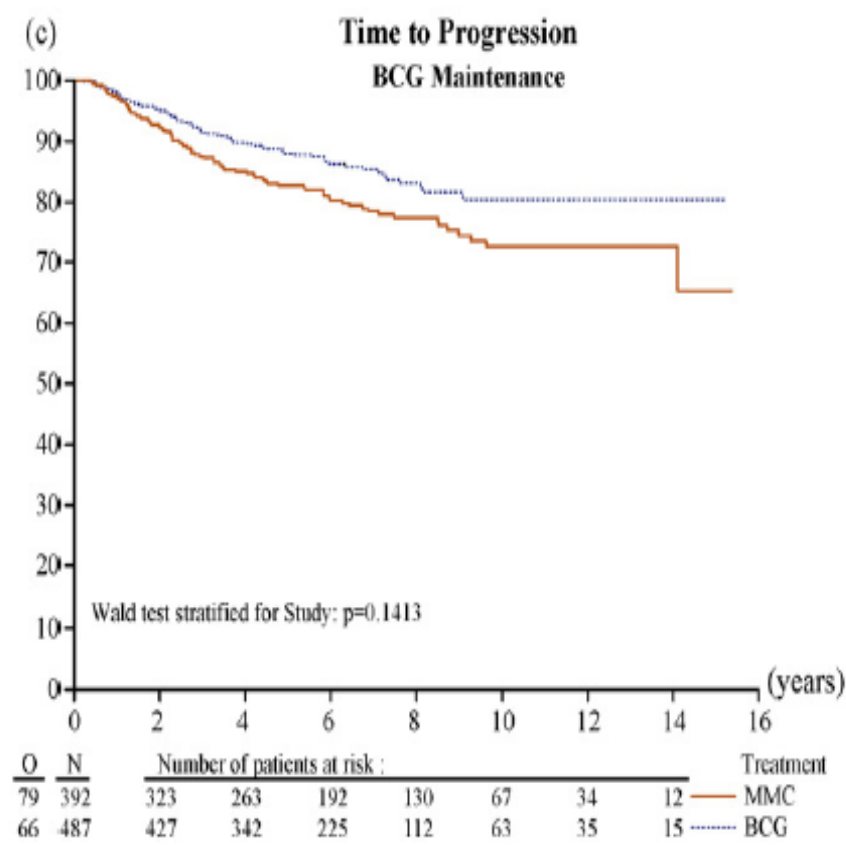
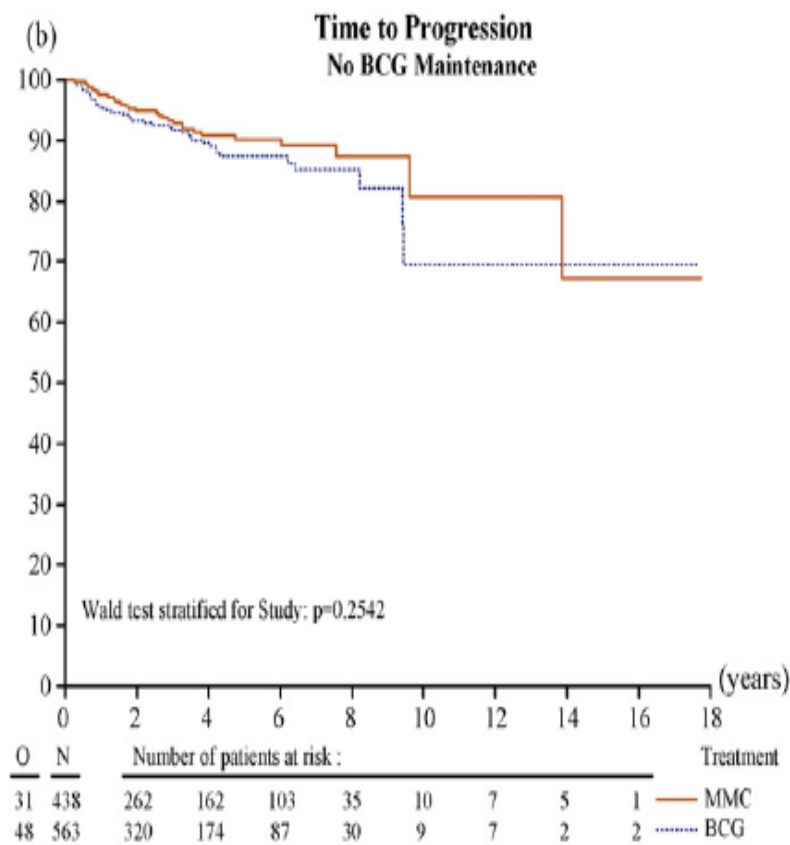
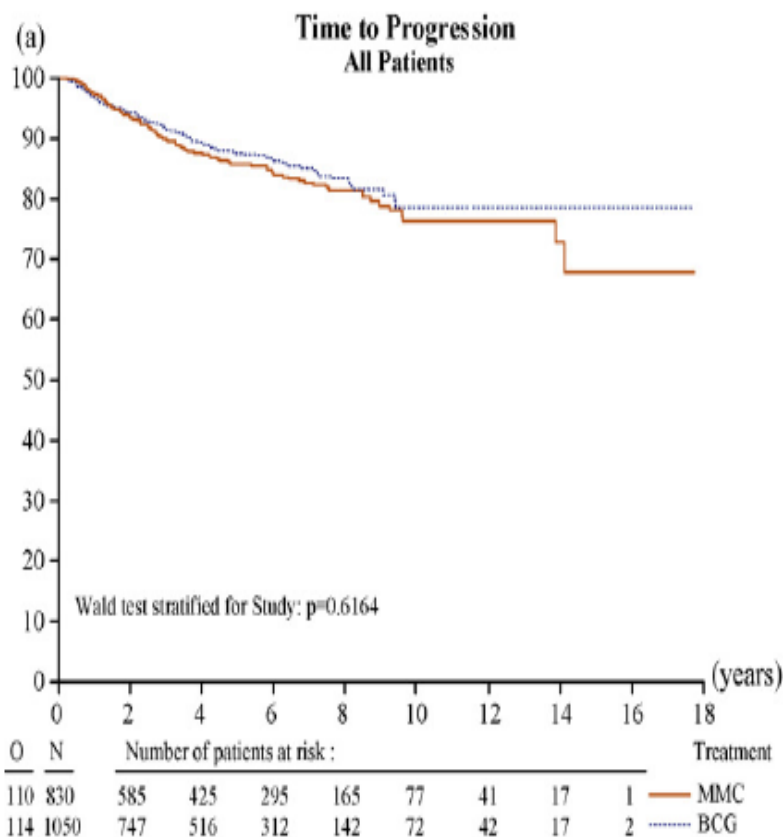
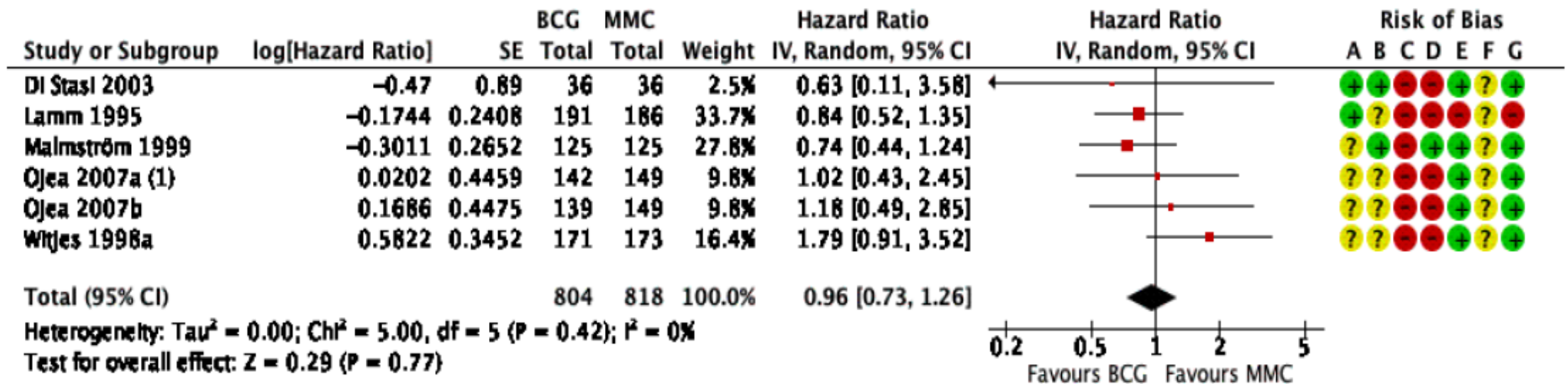




Figure 8. Forest plot of comparison: 1 Bacillus Calmette-Guérin (BCG) versus mitomycin C (MMC), outcome: 1.4 Time to progression.



Time to progression: BCG may make little or no difference on time to progression compared to MMC (HR 0.96, 95% CI 0.73 to 1.26; participants = 1622, studies = 6; 804 participants in the BCG arm and 818 in the MMC arm; low-certainty evidence). This corresponds to four fewer progressions (29 fewer to 27 more) with BCG at five years.



... toxicity

A systematic review of intravesical bacillus Calmette-Guérin plus transurethral resection vs transurethral resection alone in Ta and T1 bladder cancer



M.D. SHELLEY, H. KYNASTON*, J. COURT, T.J. WILT†, B. COLES, K. BURGON and M.D. MASON

Table 4 The BCG strain, dose and schedule of administration for the six trials, and the reported toxicities induced by intravesical BCG

<i>Trial</i>	<i>[12]</i>	<i>[13]</i>	<i>[14]</i>	<i>[15]</i>	<i>[16]</i>	<i>[17]</i>
BCG strain	P(C)	P	P	P(AF)	P	Tokyo
Weekly dose, mg	120	120	75	120	150	80
c.f.u. × 10 ⁸	NR	NR	4–5	NR	6	NR
Duration of instillation (h)	1	2	2	2	2	2
Schedule, × weekly	× 6,	× 6	× 6*	× 6	× 8	× 6
plus monthly	× 4					× 2 for 6
Subcutaneous/percutaneous, mg	0.5	5	no c.f.u.	5 × 10 ⁷	no	× 20
						no
Toxicity (mean %)						
Cystitis	34	93	27	88	84	76 (67)
Haematuria	6	34	3	58	21	14 (23)
Fever	18	28	16	44	27	14 (25)
Frequency	–	90	–	51	–	– (71)
Flu-like	–	7	–	28	10	– (15)
Nausea	–	11	–	5	7	– (8)
Malaise	–	10	–	26	7	– (14)
Prostatitis	5	1	2	2	1	– (3)
Epididymitis	10	1	2	–	–	– (6)
Allergic	3	–	–	19	–	– (10)
BCG-induced cystectomy	1	–	–	–	–	– (<1)
‘BCG-itis’	–	0	0	0	–	–
Deaths	0	0	0	0	0	0
Contracted bladder	–	0	1	0	–	10

*If no tumour was found after the weekly dose, then BCG was given monthly × 12 followed by 3-monthly × 3, if tumour was present an additional 6 weeks of BCG was given. P, Pasteur; (C), Connaught; AF, Armand Frappier; NR, not reported.



Management options for local side effects (modified from IBCG)	
Symptoms of cystitis	Phenazopyridine, mirabegron or NSAIDs.
	If symptoms improve within a few days: continue instillations.
	If symptoms persist or worsen: a. Postpone the instillation b. Perform a urine culture c. Start empirical antibiotic treatment.
	If symptoms persist even with antibiotic treatment: a. With positive culture: adjust antibiotic treatment according to sensitivity. b. With negative culture: quinolones* and potentially analgesic anti-inflammatory instillations once daily for five days (repeat cycle if necessary).
	**If symptoms persist: anti-TB drugs + corticosteroids.
	If haematuria persists, perform cystoscopy to evaluate presence of bladder tumour.
Haematuria	Perform urine culture to exclude haemorrhagic cystitis if other symptoms present.
	If haematuria persists, perform cystoscopy to evaluate presence of bladder tumour.
Symptomatic granulomatous prostatitis	Perform urine culture.
	Quinolones.
	If quinolones are not effective: isoniazid (300 mg/day) and rifampicin (600 mg/day) for three months.
	Cessation of intravesical therapy.
Epididymo-orchitis [391]	Perform urine culture and administer quinolones.
	Cessation of intravesical therapy.
	Orchidectomy if abscess or no response to treatment.

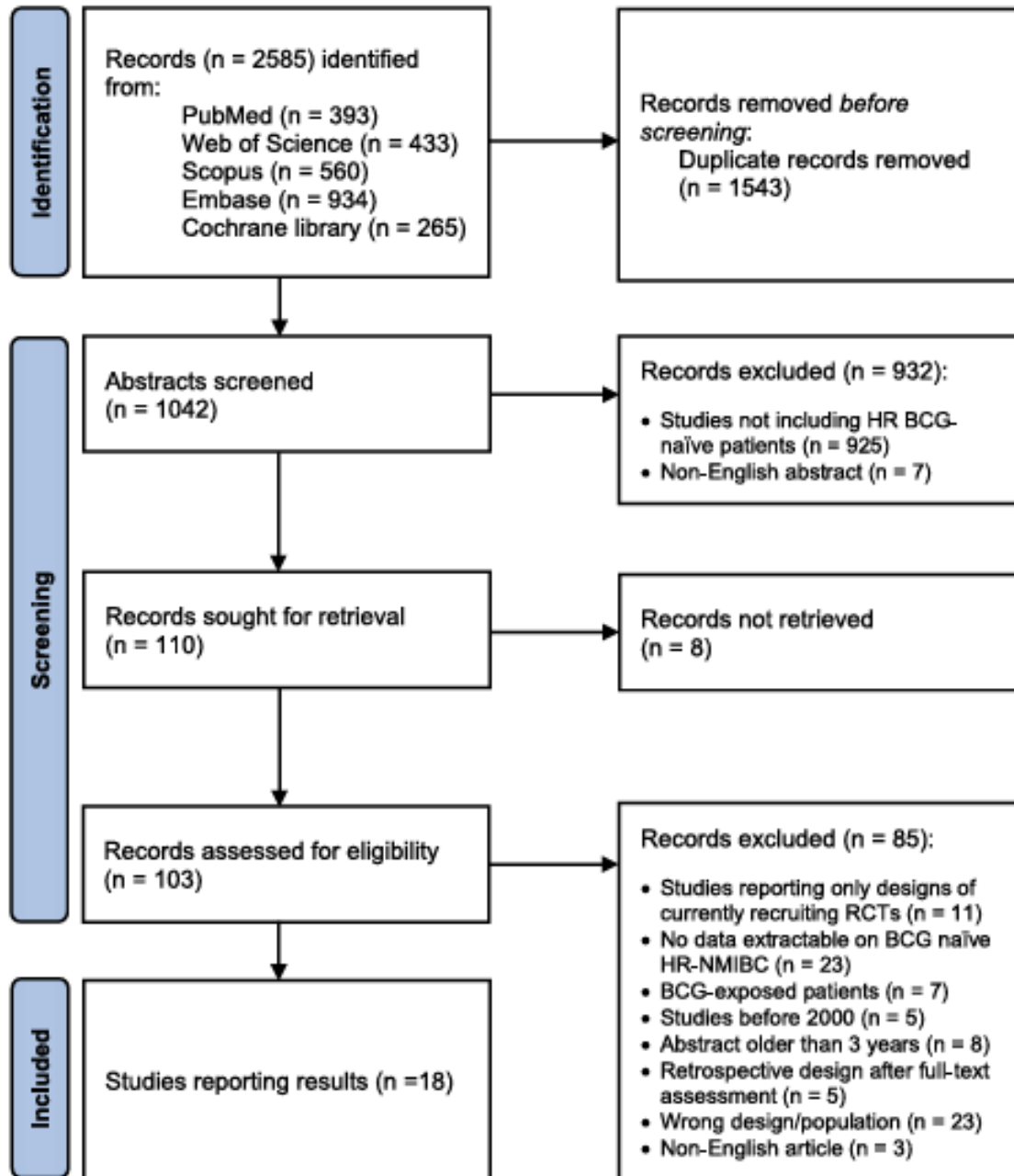
Management options for systemic side effects	
General malaise, fever	Generally resolve within 48 hours, with or without antipyretics.
Arthralgia and/or reactive arthritis	Rare complication and considered autoimmune reaction.
	Arthralgia: treatment with NSAIDs.
	Reactive arthritis: NSAIDs.
	If no/partial response, proceed to corticosteroids, high-dose quinolones or anti-TB drugs.
Persistent high-grade fever ($> 38.5^{\circ}\text{C}$ for > 48 h)	Permanent discontinuation of BCG instillations.
	Immediate evaluation: urine culture, blood tests, chest X-ray.
	Prompt treatment with more than two antimicrobial agents while diagnostic evaluation is conducted.
	Consultation with an infectious disease specialist.
BCG sepsis	Prevention: initiate BCG at least two weeks post-TURBT (if no signs and symptoms of haematuria).
	Cessation of BCG.
	For severe infection: • High-dose quinolones or isoniazid, rifampicin, and ethambutol 1.2 g daily for six months. • Early, high-dose corticosteroids as long as symptoms persist. • Consider an empirical non-specific antibiotic to cover Gram-negative bacteria and/or <i>Enterococcus</i>.
Allergic reactions	Antihistamines and anti-inflammatory agents.
	Consider high-dose quinolones or isoniazid and rifampicin for persistent symptoms.
	Delay therapy until reactions resolve in case of mild (local) reaction. Discontinue BCG in case of moderate- or severe systemic reaction.



... alternatives ?

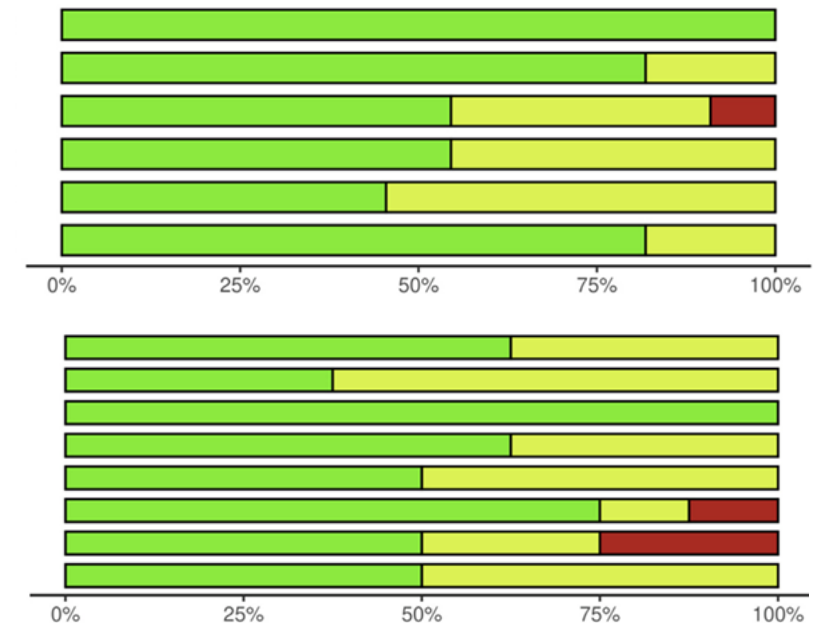


Identification of studies via databases and other methods



Oncological Outcomes in Bacillus Calmette-Guérin-naïve High-risk Non-muscle-invasive Bladder Cancer Patients: A Systematic Review on Current Treatment Strategies and Future Perspectives

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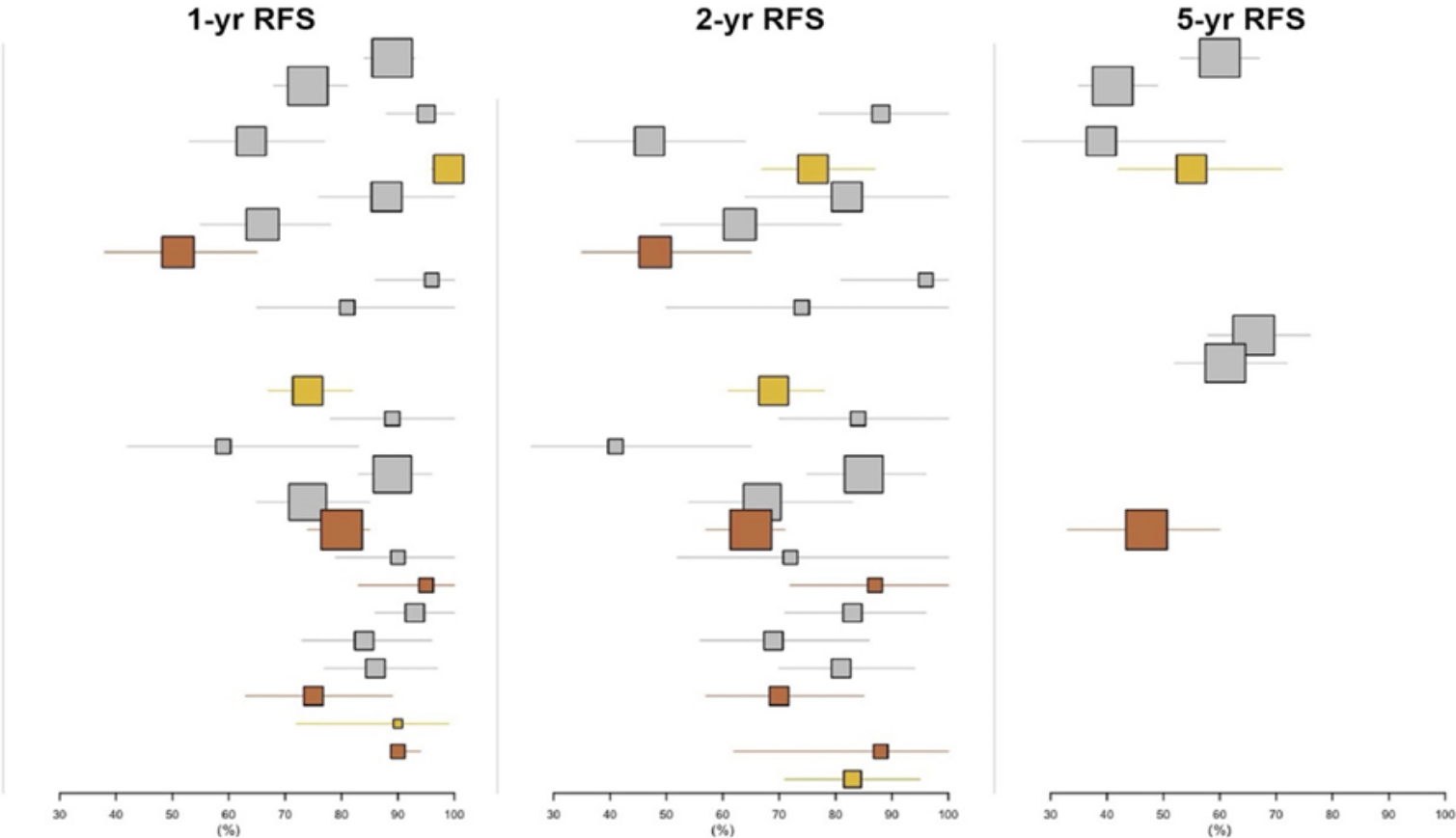
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Lamm et al , 2000 (SWOG-8507) (I)
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 Gan et al., 2016
 Mohamed et al., 2020 (I)
 Mohamed et al., 2020 (C)
 Grimm et al. 2020 (C)
 Grimm et al. 2020 (I)
 Plata et al , 2021 (HIVEC-E)
 Guerrero-Ramos et al , 2022 (HIVEC-HR) (C)
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 Zaza et al , 2024 (C)
 Zaza et al , 2024
 Wang et al , 2024
 Patel et al , 2024
 Guerrero-Ramos et al , 2024 (BladderGATE)

BCG (i + m)
 BCG (i)
 BCG (i + m)
 BCG (i)
 BCG + EMDA MMC
 BCG (i + m)
 BCG (i + m)
 Epi + IFN-α2β
 BCG (i + m)
 BCG (i)
 BCG (i + m)
 BCG (i)
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 BCG (i + m)
 BCG (i)
 BCG (i + m)
 BCG (i + m)
 HIVEC MMC
 BCG (i + m)
 HIVEC MMC
 BCG (i + m)
 BCG (i)
 BCG (i + m)
 MMC
 BCG + Epi + Cis + tislelizumab
 Gem/Doce
 BCG + atezolizumab



Studies included	n	1-yr RFS	2-yr RFS	5-yr RFS
12 BCG-treated	1418	66–96%	63–96%	39–66%
9 No BCG-treated	657	51–99%	48–88%	47–55%



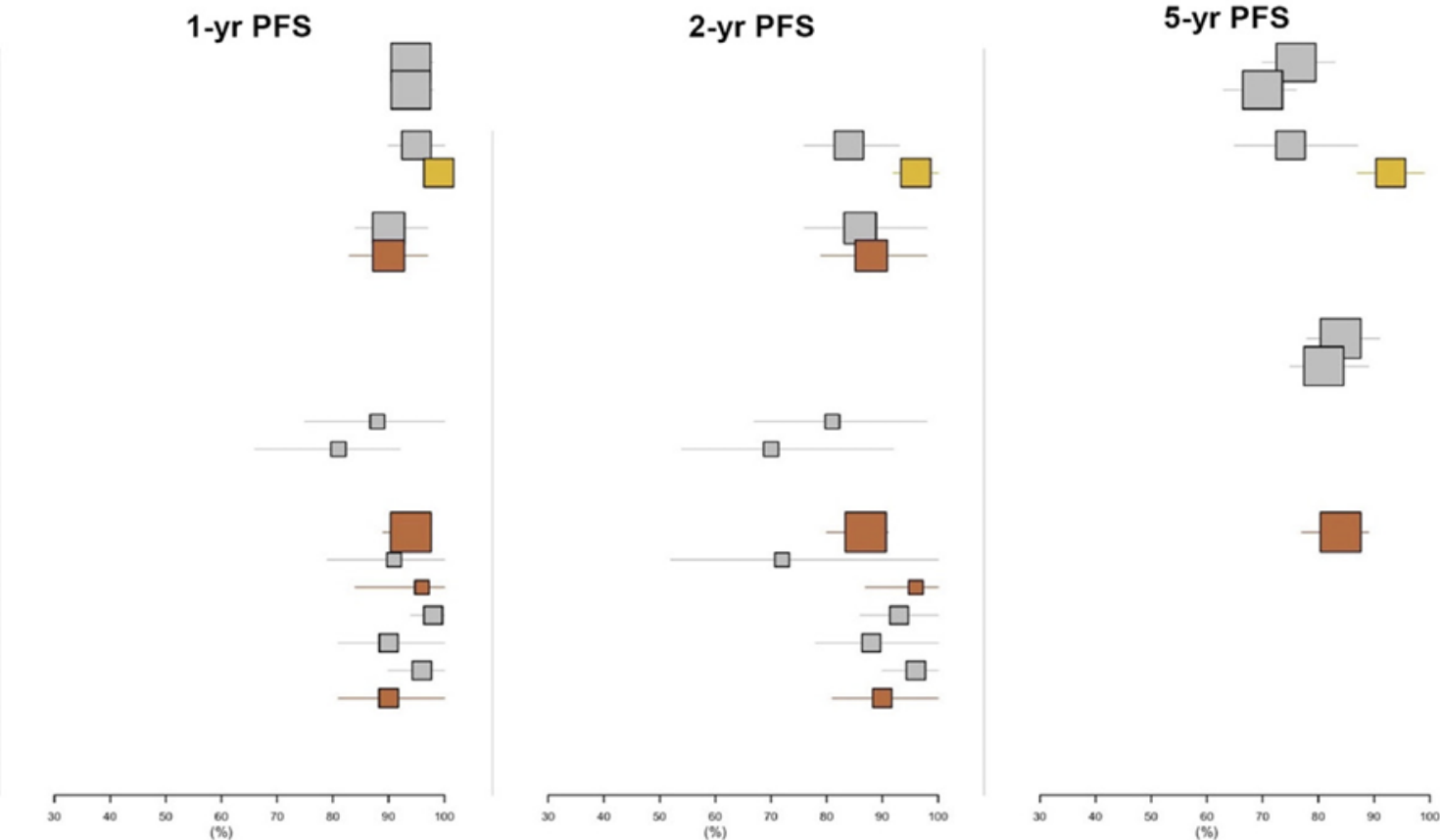
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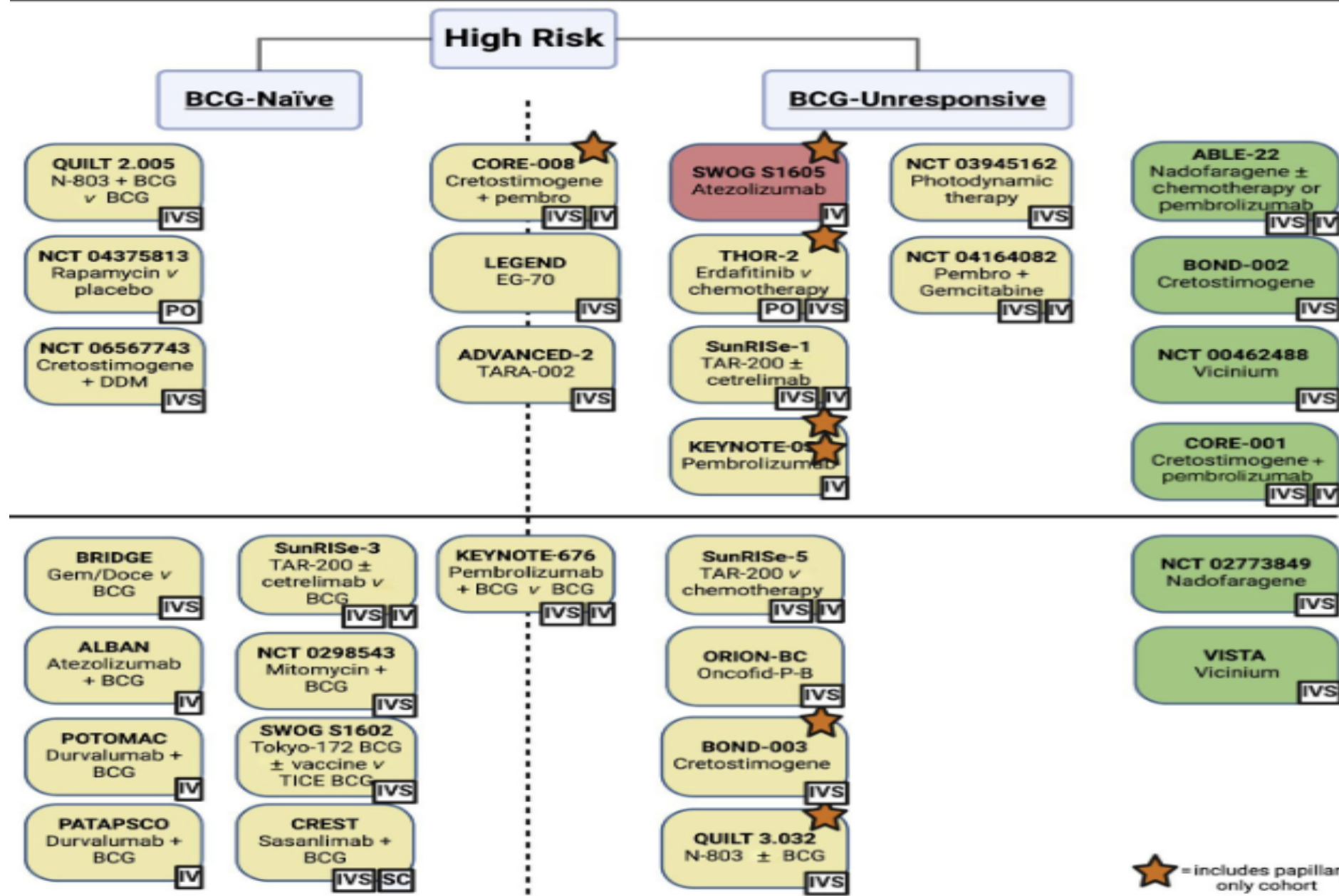
Studies included	n	1-yr PFS	2-yr PFS	5-yr PFS
12 BCG-treated	1418	81–98%	70–96%	70–84%
9 No BCG-treated	657	90–100%	88–96%	84–93%

NEW

MasterClass in Bladder Cancer 2026

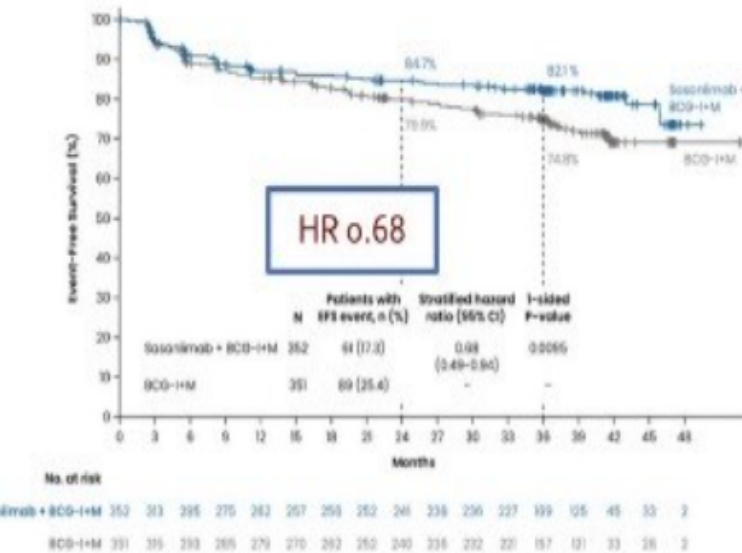
Phase II

Phase III





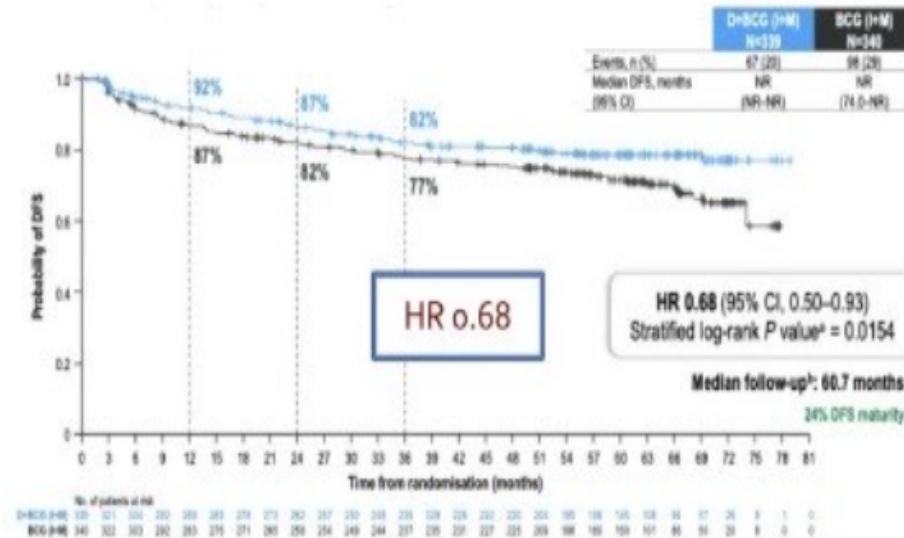
CREST



Grade ≥ 3 TrAE: 6% vs 29%

N Shore et al., Nat Med 2025

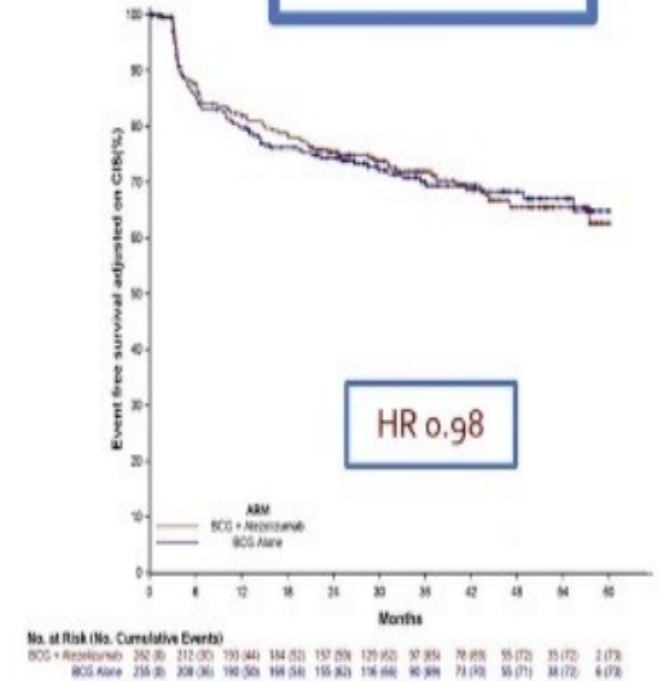
POTOMAC



Grade ≥ 3 TrAE: 4% vs 21%

M De Santis et al., Lancet Oncol 2025

ALBAN



Grade ≥ 3 TrAE: 9% vs 23%

M Roupret et al., Annals Oncol 2025



Recommendations	Strength rating
<i>European Association of Urology (EAU) risk group: Low</i>	
Offer one immediate instillation of intravesical chemotherapy after transurethral resection of the bladder tumour (TURBT).	Strong
<i>EAU risk group: Intermediate</i>	
In general, chemotherapy (the optimal schedule is unknown) is a reasonable first-line option in the majority of patients. One-year full-dose Bacillus Calmette-Guérin (BCG) treatment (induction plus three-weekly instillations at 3, 6 and 12 months), is an alternative option. The final choice should reflect the individual patient's risk of recurrence and progression.	Strong

EAU risk group: High

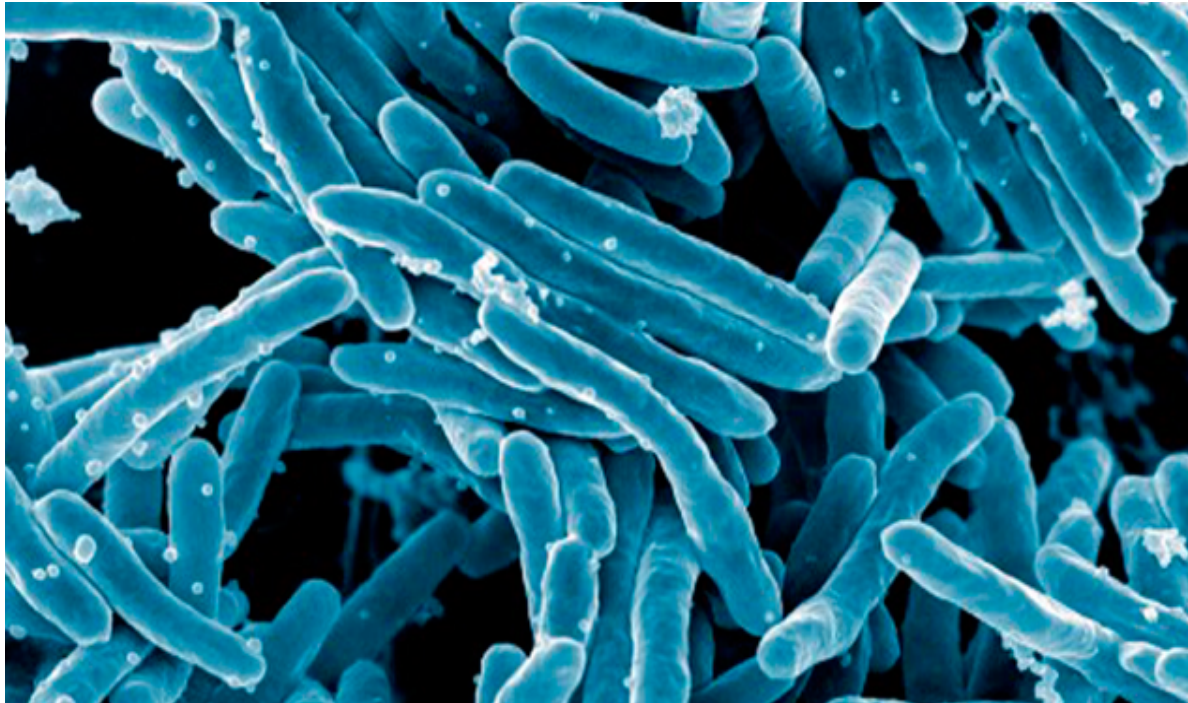
Offer intravesical full-dose BCG instillations for one to three years but discuss immediate radical cystectomy (RC).

Strong

EAU risk group: Very high

Offer RC or intravesical full-dose BCG instillations for one to three years, particularly to those who decline or are unfit for RC.

Strong



...Gracias

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Bladder Cancer 2026

June 9th

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