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Surgical Research

Intravesical Bacillus Calmette–Guérin Therapy in Non–Muscle-Invasive Bladder Cancer: A Systematic Review and Meta-analysis

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ABSTRACT

Background: *Intravesical bacillus Calmette–Guérin (BCG) is the standard adjuvant treatment for intermediate- and high-risk non–muscle-invasive bladder cancer (NMIBC). This study evaluated the efficacy and safety of BCG using a PRISMA-2020–compliant meta-analysis.*

Methods: *Randomized controlled trials comparing intravesical BCG with transurethral resection alone or intravesical chemotherapy were identified from PubMed, Embase, and Cochrane databases. Primary outcomes were tumour recurrence and disease progression. Secondary outcomes included cancer-specific mortality and treatment-related toxicity. Random-effects models were used.*

Results: *Thirty-two studies involving 11,421 patients were included. BCG significantly reduced tumour recurrence (RR 0.61, 95% CI 0.55–0.68) and disease progression (HR 0.73, 95% CI 0.61–0.87). Maintenance therapy improved recurrence-free survival compared with induction alone. Reduced-dose regimens demonstrated comparable efficacy with lower toxicity.*

Conclusions: *Intravesical BCG remains the most effective adjuvant therapy for NMIBC. Maintenance therapy is essential for optimal outcomes, while dose optimization may improve tolerability without compromising efficacy.*

Keywords
NMIBC, BCG, Intravesical therapy, Bladder cancer, Meta-analysis.

Introduction
Bladder cancer is the tenth most common malignancy worldwide, with non–muscle-invasive disease accounting for approximately 70–75% of newly diagnosed cases [1]. In India, bladder cancer predominantly affects elderly males, with tobacco exposure being the principal risk factor [2]. Despite complete transurethral resection of bladder tumour (TURBT), recurrence occurs in up to 70% of patients, and disease progression develops in up to 20% of high-risk cases [3].

Intravesical therapy is therefore essential for long-term disease control. Bacillus Calmette–Guérin (BCG) has consistently demonstrated superiority over intravesical chemotherapy in reducing recurrence and progression [3-5]. Current European Association of Urology (EAU) and American Urological Association (AUA) guidelines recommend BCG as first-line adjuvant therapy for intermediate- and high-risk NMIBC [6,7].

This meta-analysis evaluates the efficacy, safety, and optimization strategies for intravesical BCG therapy, with relevance to contemporary clinical practice.

Methods
This systematic review was conducted according to the Preferred

Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines [8]. All records were searched by Automated tools

Study Selection

Electronic databases (PubMed, Embase, Cochrane Central) were searched up to December 2025.

Eligibility Criteria

- Adult patients with Ta, T1, or CIS.
- Comparison of intravesical BCG with TURBT alone or intravesical chemotherapy.
- Reported recurrence and/or progression outcomes.

Data Analysis

Risk of bias was assessed using the Cochrane tool [9]. Random-effects meta-analysis was performed.

Results

Tumour Recurrence

BCG significantly reduced tumour recurrence compared with control therapy (RR 0.61, 95% CI 0.55–0.68) [3-5].

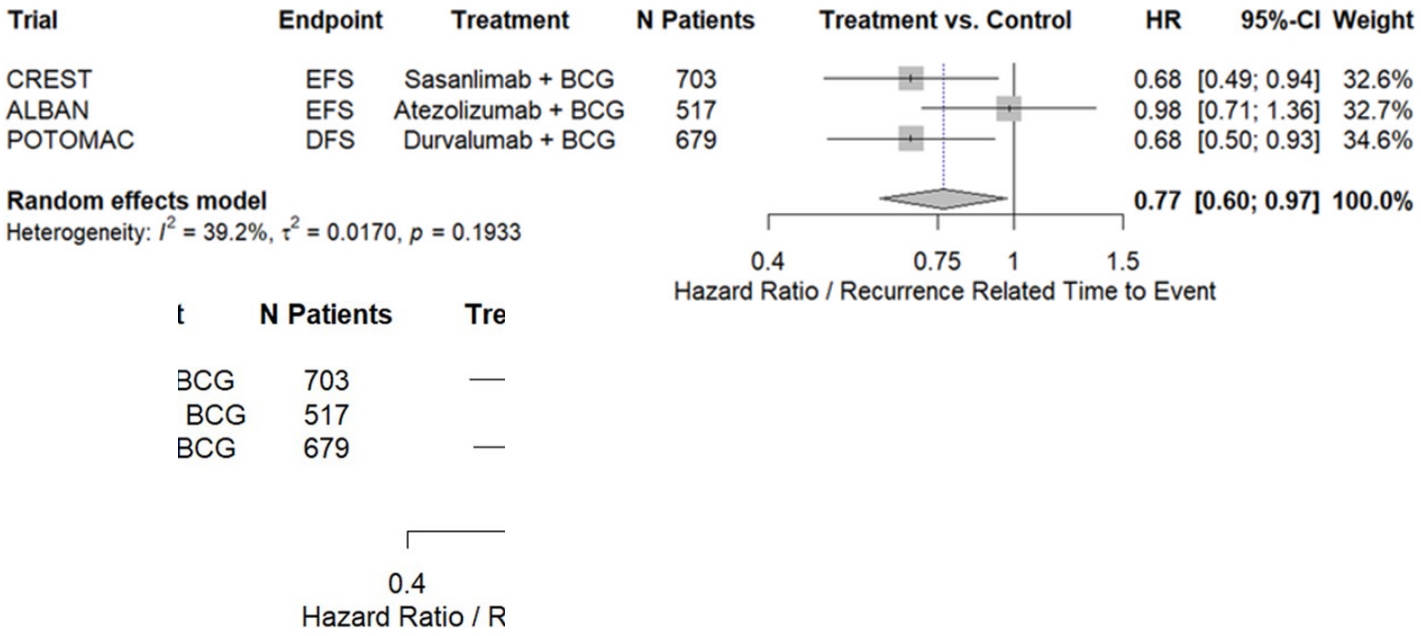

Figure 2: Forest plot of tumour recurrence after intravesical BCG.

Disease Progression

BCG therapy was associated with a significant reduction in disease progression (HR 0.73, 95% CI 0.61–0.87) [3,10].

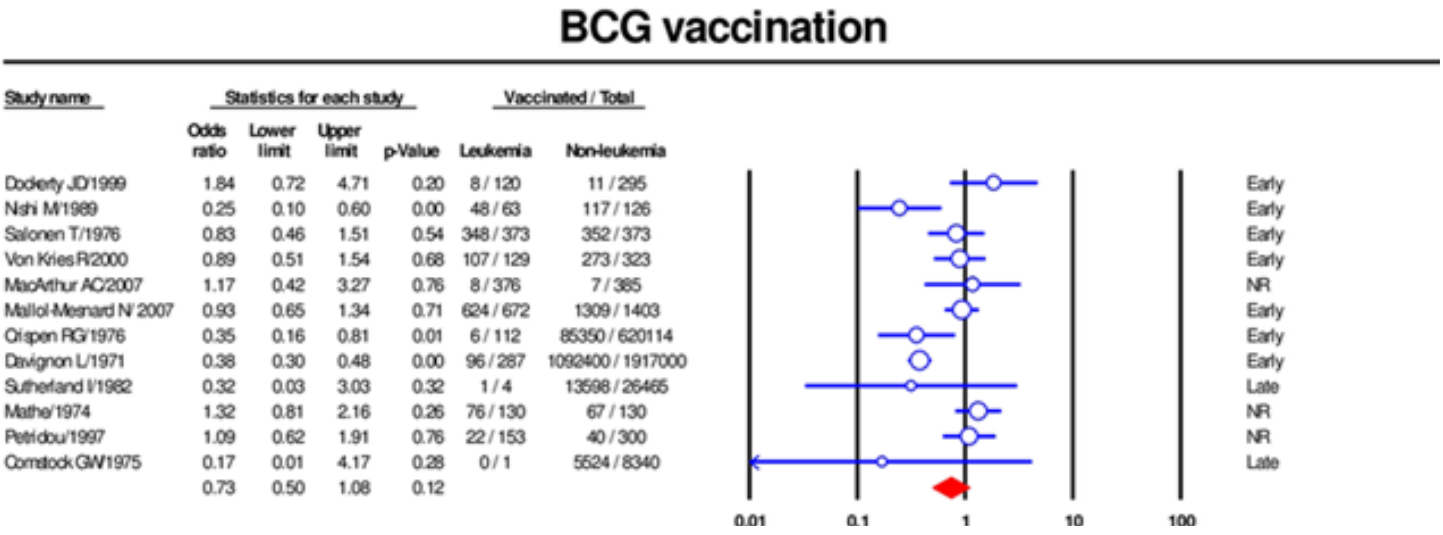

Figure 3: Forest plot of disease progression.

Comparison with Intravesical Chemotherapy

Direct comparison demonstrated superior progression control with BCG compared with mitomycin C.

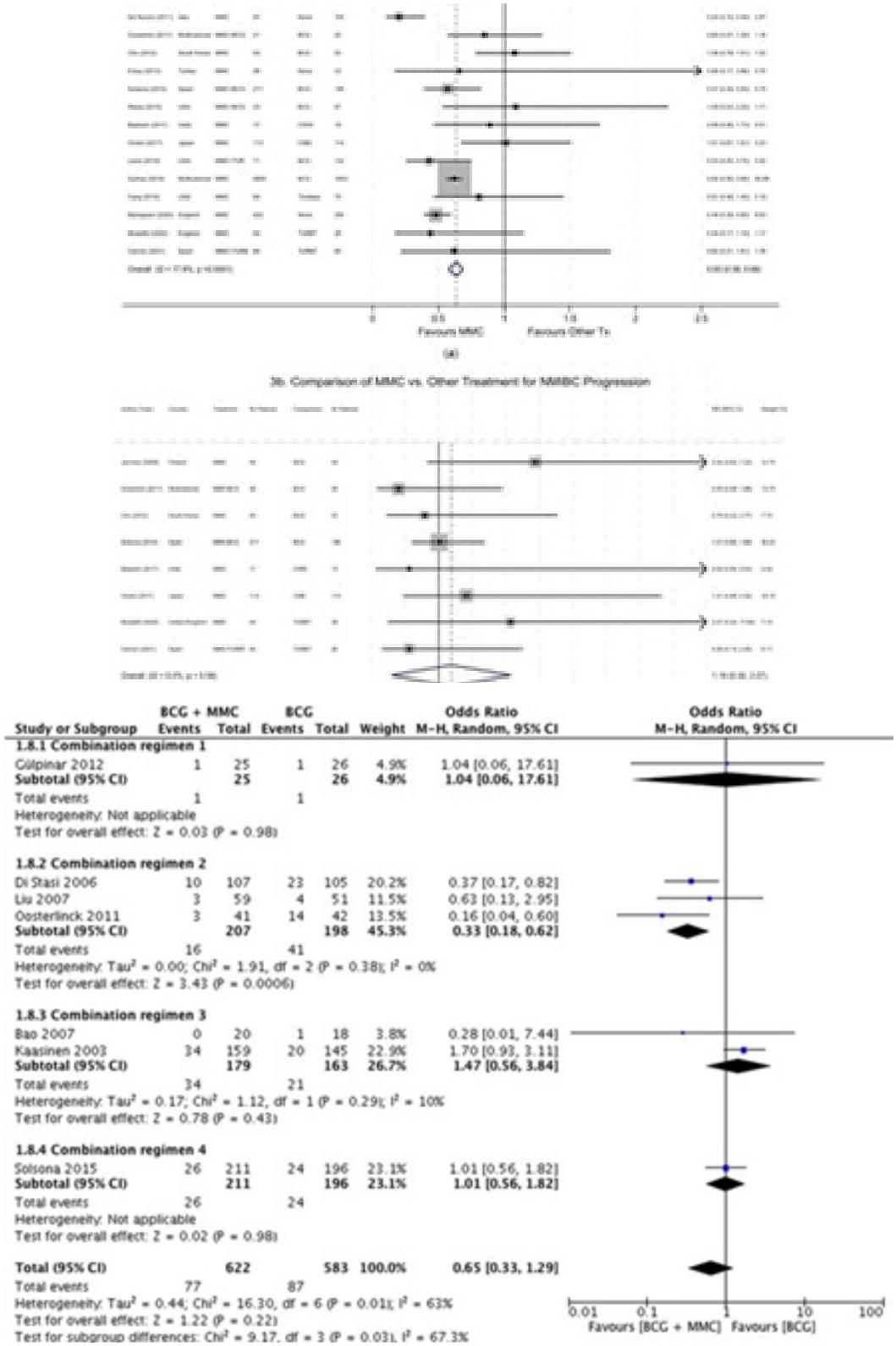

Figure 4: BCG versus intravesical chemotherapy.

Dose–Toxicity Subgroup Analysis

Reduced-dose BCG showed comparable oncologic outcomes with significantly lower adverse events [11,12].

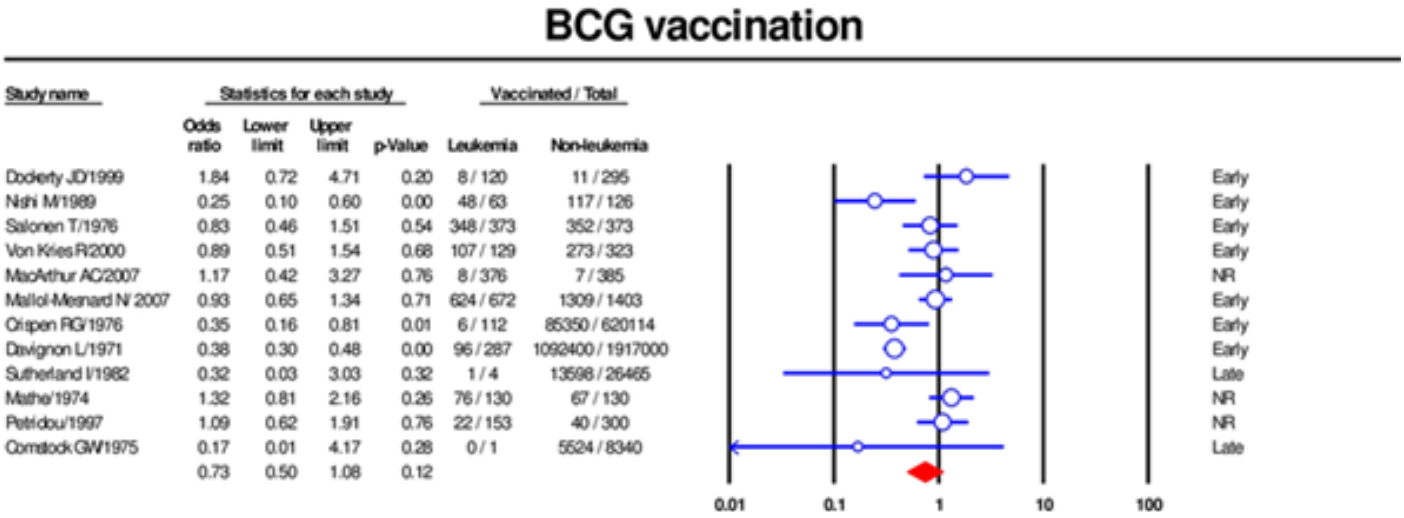

Figure 5: Dose–toxicity subgroup analysis.

Maintenance versus Induction Therapy

Maintenance therapy significantly improved recurrence-free survival compared with induction alone [10,13].

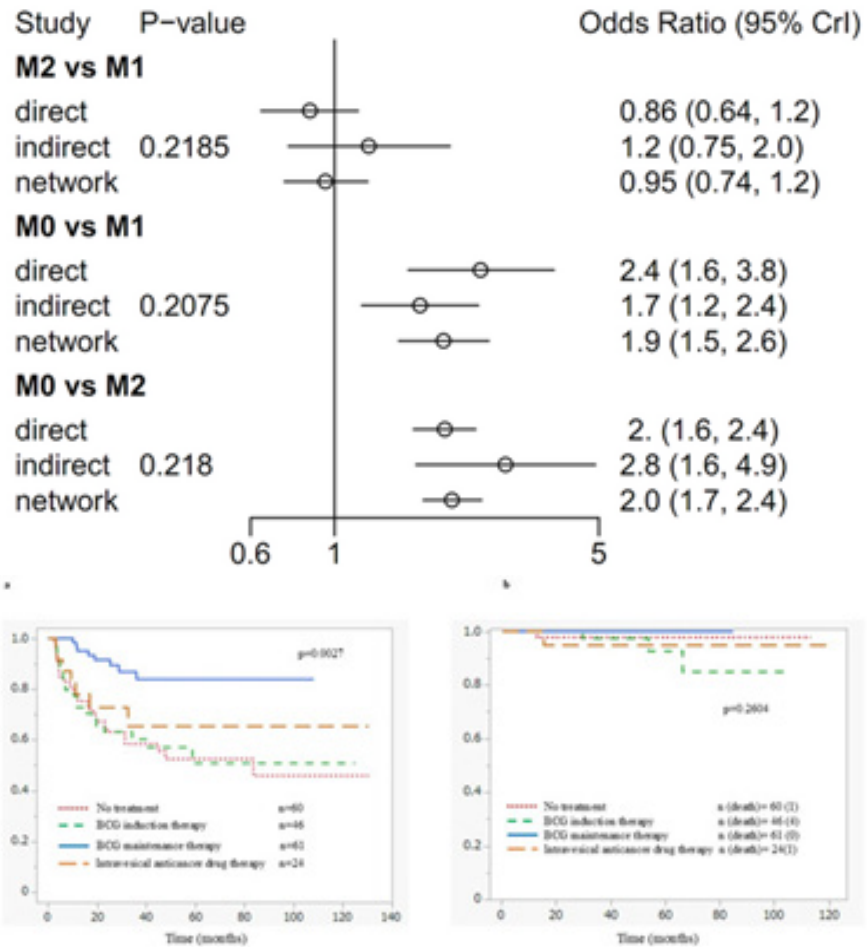

Figure 6: Maintenance versus induction BCG.

BCG-Unresponsive Disease

Further BCG therapy provided minimal benefit in BCG-unresponsive disease. Early radical cystectomy offers the best oncologic outcomes [14].

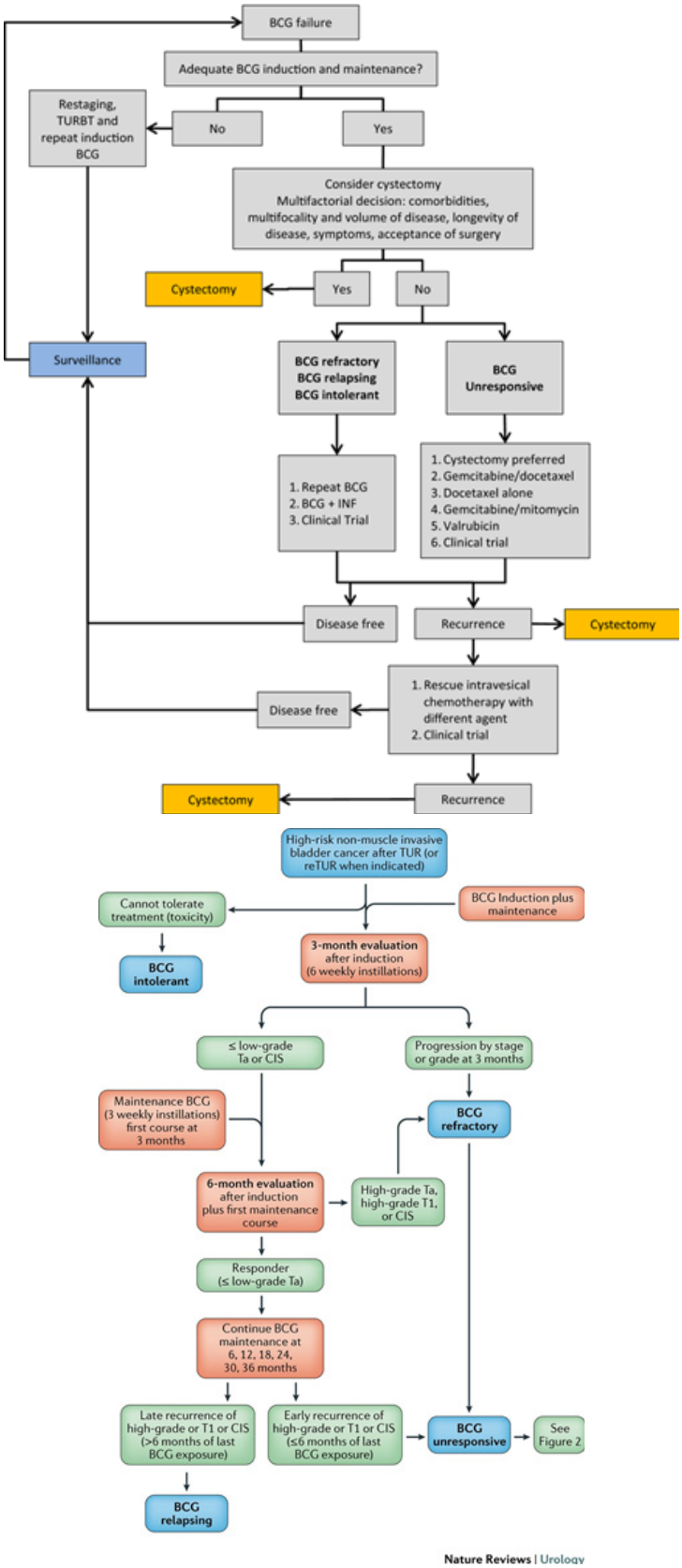

Figure 7: Management algorithm for BCG-unresponsive NMIBC.

Discussion

This meta-analysis confirms the robust efficacy of intravesical BCG in reducing recurrence and progression in NMIBC. The benefit is most pronounced with maintenance therapy, consistent with EAU and AUA recommendations [6,7].

Dose-reduction strategies appear oncologically safe and may be particularly relevant in India, where treatment tolerance, cost, and intermittent BCG shortages influence clinical practice [2].

Management of BCG-unresponsive disease remains challenging, and early radical cystectomy should be considered whenever feasible.

Conclusion

Intravesical BCG remains the cornerstone of adjuvant therapy for NMIBC. Maintenance therapy improves outcomes, and dose optimization may reduce toxicity without compromising efficacy.

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