Adding mitomycin (MM) to Bacillus Calmette-Guérin (BCG) as adjuvant intravesical therapy for high-risk, non muscle-invasive urothelial bladder cancer (NMIBC)

(BCGMM; ANZUP 1301)

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1. Background and Rationale

- Adjuvant intravesical BCG decreases recurrence and progression in high-risk NMIBC, however recurrence occurs in 30% of those affected, despite optimal therapy.
- Phase 2 study and meta-analyses evaluating administration of both intravesical BCG and chemotherapy showed lower rates of recurrence and cancer-specific mortality in people with NMIBC who received these regimens.
- This trial is the largest randomized study to date evaluating this approach in high-risk NMIBC.
- This trial is of particular relevance given the current BCG shortage.
- If this approach is efficacious it has the potential to change global practice, the number of patients requiring radical cystectomy, irradiation, and systemic chemotherapy may be reduced.

2. Aim

To determine the effects of adding intravesical MM to standard intravesical therapy with BCG after resection of high-risk NMIBC.

3. Study Design

Design: Open-label, stratified, 2-arm, 2 stage multi-center phase 3 trial randomizing participants in a 1:1 ratio to receive intravesical BCG in the standard arm or intravesical BCG and MM in the experimental arm.

Stratification: Stage, site of disease, and presence of carcinoma in-situ.

Target Population: Participants with resected high-risk NMIBC suitable for BCG (high grade Ta or any grade T1).

Sample Size: 130 participants in Stage 1 gives 95% power to distinguish completion rates of ≥70% (satisfactory) versus ≤50% (unsatisfactory) in each arm at a significance level of 5%.

A further 370 participants in Stage 2 to make up a sample size of 500 gives 85% power to detect a 10% improvement in 2-year DFS at a significance level of 5%.

4. Study Objectives (endpoints):

Stage 1 primary:	Rates of treatment completion.
Stage 2 primary:	Disease free survival (evidence of urothelial carcinoma or death).
Secondary:	Activity (no recurrence on cystoscopy at 3 months). Time to recurrence (recurrence of urothelial carcinoma, TTR). Time to progression (recurrence of higher grade or stage, TTP). Safety (AE according to CTCAE v4.03). Health-related quality of life (QLQ-BLS24, QLQ-C30, I-PSS). Overall survival (death from any cause). Feasibility (compliance with intravesical therapy). Marginal resource use (e.g. number of visits to GP, ED, admissions)
Tertiary:	Exploratory biomarkers for potential prognostic or predictive biomarkers of treatment.

5. Study Schema

	Induction										Maintenance										
Arm A	B	B	B	B	B	B					B	B	B	B	B	B	B	B	B	B	
Weeks	1	2	3	4	5	6	7	8	9	11	13	17	21	25	29	33	37	41	45	49	52
								Cystoscopy and biopsy before 3 months →						← Cystoscopy and biopsy at 6 and 9 months →						Cystoscopy and biopsy after 12 months	
Arm B	B	B	M	B	B	M	B	B	M		M	M	B	M	M	B	M	M	B		
Weeks	1	2	3	4	5	6	7	8	9	11	13	17	21	25	29	33	37	41	45	49	52

Arm A = Standard
Arm B = Experimental

B = BCG
M = MM

6. Study Progress

Enrolment opened:	Dec 2013
Sites open to recruitment (17):	16 ANZ 1 UK
Patients recruited:	N = 500
Stage 1 Analysis (N = 130)	Successful treatment completion achieved by 76% in BCGMM group versus 60% in the BCG alone.
Stage 2 Analysis (N = 500)	Recruitment completed 10 May 2023

7. Contact us

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