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)

1. BACKGROUND AND RATIONALE

- Adjuvant intravesical BCG decreases recurrence and progression in people with high-risk NMIBC, however recurrence occurs in 30% despite optimal therapy.
- Meta-analyses evaluating the addition of intravesical MM to BCG showed lower rates of recurrence and cancer-specific mortality in people with NMIBC who received combination regimens.
- The BCGMM trial will be the largest randomized study to date evaluating this approach in people with high-risk NMIBC.
- If this approach is efficacious, the number of patients requiring radical cystectomy, irradiation, and systemic chemotherapy will 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 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.

4. STUDY OBJECTIVES

Stage 1 primary objective: Rates of treatment completion.
Stage 2 primary objective: Disease free survival defined by evidence of transitional cell carcinoma (TCC) or death.
Secondary objectives:
- Activity (no recurrence on cystoscopy at 3 months)
- Time to recurrence of TCC
- Time to progression
- Safety
- Health-related quality of life
- Overall survival
- Feasibility

Tertiary objectives:
- Exploratory biomarkers studies for potential prognostic or predictive biomarkers of treatment.

5. STUDY SCHEMA

<table>
<thead>
<tr>
<th>Induction</th>
<th>Maintenance</th>
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<tbody>
<tr>
<td>Arm A</td>
<td>B B B B B B</td>
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<tr>
<td>Weeks</td>
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<td>Cystoscopy and biopsy before 3 months</td>
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<td>Cystoscopy and biopsy at 6 and 9 months</td>
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Cystoscopy and biopsy after 12 months

Arm A = Standard
Arm B = Experimental

Arm A: BCG, Arm B: BCGMM

Stage 1 of the study has completed, with 228 participants recruited from 13 sites. Successful treatment completion has been achieved in 76% of patients treated in the experimental arm of Stage 1, compared to 60% in those allocated BCG alone.

6. STUDY PROGRESS

As of 17 December 2019, 228 participants have been recruited from 13 sites. Successful treatment completion has been achieved in 76% of patients treated in the experimental arm of Stage 1, compared to 60% in those allocated BCG alone.

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This study is being conducted by ANZUP in collaboration with the National Health and Medical Research Council (NHMRC) Clinical Trials Centre at the University of Sydney. ANZUP is supported by the Australian Government through Cancer Australia. Clinical trial identification number: NCT02948543. Australian New Zealand Clinical Trials Registry ACTRN12613000513718. For all trial enquiries: bcgmmc@ctc.usyd.edu.au

Cystoscopy and biopsy at 6 and 9 months

Cystoscopy and biopsy before 3 months

Cystoscopy and biopsy after 12 months

Scan for ANZUP
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