EAU23

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Cutting-edge Science at
Europe's largest Urology Congress

Adding Mitomycin to BCG as adjuvant intravesical therapy for high-risk, non-muscle-invasive-bladder cancer: a randomised phase 3 trial: The BCG+MM Trial (ANZUP 1301)

Hayne D., Stockler M., Martin A.J., Mccombie S., Zebic D., Krieger L., Anderson P., Bastick P., Beardsley E., Blatt A., Frydenberg M., Green W., Grummet J., Hawks C., Ischia J., Mitterdorfer A., Patel M., Roberts M., Sengupta S., Srivastav R., Winter M., Redfern A.D., Davis I.D.

On behalf of Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP)

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European Association of Urology

Conflict of Interest Disclosure

I have the following potential conflict(s) of interest to report:

- **Advisory Boards**
  - Abbott (H)
  - Janssen (H)
  - Tolmar (H)
  - Urogen (O)
  - BMS (O)
  - Pacific Edge (O)
- **Research Funding/Support**
  - Telix (O)
  - AstraZeneca (O)
- **Travel / Meeting Support**
  - AstraZeneca (H)
  - Mundipharma (H)
  - Novartis (H)
  - Abbott (H)
  - Telix
- **Speaker Meetings**
  - GSK (H)
  - Abbvie (H)
  - Novartis (H)

Funding and Support

- 'The BCG+MM Trial' (ANZUP-1301) is funded via competitive research grants from:
  - Cancer Australia (Stage 1)
  - National Health and Medical Research Council (NHMRC) (Stage 2)
  - ANZUP and ANZUP's 'Below the Belt' Research Fund

- We acknowledge:
  - Omegapharm™ for providing discounted mitomycin for the study
  - MSD ™ for supporting ongoing BCG supply (Oncotice ™) for this trial during the global shortage.

Background

- Adjuvant intravesical BCG with maintenance reduces disease recurrence and progression in people with high-risk NMIBC, however recurrence occurs in 30% despite optimal therapy.
- Meta-analysis suggest sequential combination therapy (BGC+MM) may be superior to BCG alone BUT **no large high quality RCT has confirmed this**
- If this approach is efficacious:
  - Outcomes will improve
    - the number of patients requiring radical cystectomy, irradiation, and systemic chemotherapy will be reduced
    - BCG supply will be better maintained for all NMIBC patients

We aim it to determine the effects of adding intravesical MM to standard intravesical BCG therapy after resection of high-risk NMIBC is superior to BCG alone.

Phase 3 RCT

Study Population
Adults with resected, high-risk NMIBC (high grade Ta or any grade T1) suitable for intravesical chemotherapy treatment
Concurrent CIS allowed
CIS only disease excluded

RANDOMISATION

Arm A (standard)
Intravesical BCG
Induction + maintenance

Arm B (experimental)
Intravesical BCG + MMC
Induction + maintenance

Min. follow-up
3-monthly (end treatment – year 3)
6-monthly (until disease progression / death / 5 years follow-up complete)

Stratified by:
- *T-stage (pTa or pT1)*
- *CIS or no CIS*
- *Site*

	Induction										Maintenance											
Arm A	B	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

STUDY OBJECTIVES

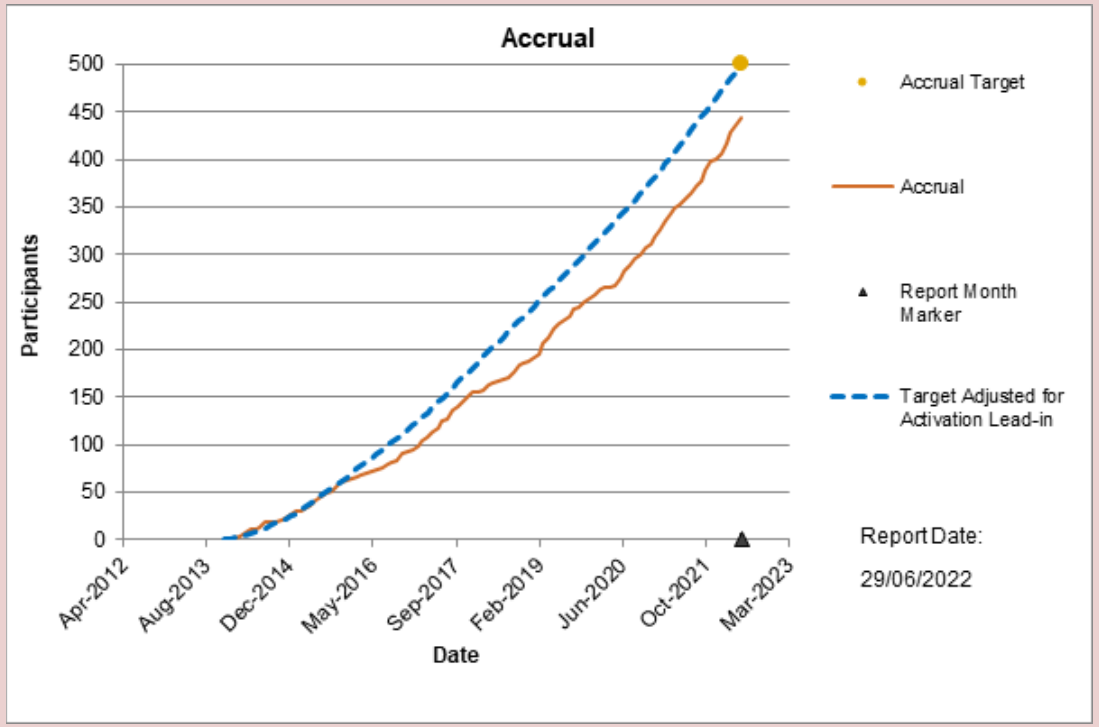
Stage 1 primary objective: **Rates of treatment completion.**

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.

Study Progress



Enrolment opened	**Dec 2013**
Sites open to recruitment (17)	**16 Aust** **1 UK**
Patients recruited	**N = 465**
Stage I Analysis (N=130)	**Successful treatment completion achieved**
Stage II analysis (N=370)	**Expected in Q1 2023**

BCGMM TRIAL PROGRESS & SIGNIFICANCE

- Meta-analysis suggest sequential combination therapy may be superior to BCG alone but this trial will provide the **first high quality test of this**
- Largest Global NMIBC Bladder Cancer Trial with >484/500 recruited
- Rich source of biomaterial for meaningful translational research
- Global BCG shortage not ending anytime soon
- If combination chemo immunotherapy more effective or equally effective with less toxicity will change paradigm for HRNMIBC treatment

Acknowledgements

We thank:

- Patients and support network
- Principle and co-investigators
- Study coordinators
- Nurses
- Clinical research associates
- Data managers
- Pharmacists

Industry support:

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