



Project title and acronym: A phase III randomized controlled trial of continuous beta-lactam infusion compared with intermittent beta-lactam dosing in critically ill patients: the Beta-Lactam Infusion Group (BLING) III study

Principal investigator/s: Professors Jeffrey Lipman, Jan De Waele & Stephen Brett et al.

Website: <https://www.georgeinstitute.org.au/projects/beta-lactam-antibiotics-infusion-group-study-bling-iii>

1. Project background/ Introduction

Due to time-dependent kill characteristics there is a strong biological precedent that continuous infusion of beta-lactam antibiotics may be substantially more effective than the historical method of intermittent infusion. However, there is clinical uncertainty as to whether beta-lactam antibiotics administered by continuous infusion result in improved outcomes for patients with sepsis compared to intermittent infusion.

2. Project Scope

A randomised controlled trial (RCT) to determine whether continuous infusion of piperacillin-tazobactam or meropenem results in decreased all-cause Day 90 mortality compared with intermittent infusion of these beta-lactam antibiotics in critically ill patients with sepsis.

3. Methodology

A prospective, multicentre, open, phase 3 RCT in 104 intensive care units in 7 countries; 7000 patients with sepsis will be randomised in a 1:1 fashion to receive the prescribed beta-lactam antibiotic by either continuous infusion (intervention arm) or intermittent infusion (control arm).

4. Results/ Expected results

Level 3 evidence of whether administration of beta-lactam antibiotics (piperacillin-tazobactam and meropenem) by continuous infusion for patients with sepsis results in improved clinical outcomes compared with intermittent infusion.

5. Timeframe

Recruitment will be completed by mid-January 2023 with 90 day-follow-up completed by mid-April 2023.

6. Additional information (if applicable)

- a. *How can I participate in the project? Not applicable (all study sites have been selected).*
- b. *Do I need an IRB approval? Yes, required for all participating sites.*
- c. *Acknowledgment (contributors and collaborators)*



BLING III Study Management Committee: Jeffrey Lipman (Chair), Stephen J. Brett, Jan J. De Waele, Menino O. Cotta, Joshua S. Davis, Simon Finfer, Naomi E. Hammond, Serena Knowles, Shay McGuinness, John A. Myburgh, David L. Paterson, Sandra Peake, Dorrilyn Rajbhandari, Andrew Rhodes, Jason A. Roberts, Claire Roger, Charudatt Shirwadkar, Therese Starr, and Colman Taylor.

Study Sponsor: The George Institute for Global Health.

7. Additional documents

Lipman J, Brett SJ, De Waele JJ, et al. A protocol for a phase 3 multicentre randomised controlled trial of continuous versus intermittent beta-lactam antibiotic infusion in critically ill patients with sepsis: BLING III. Crit Care Resusc 2019;21:63-8.

Billot L, Lipman J, Brett SJ, et al. Statistical analysis plan for the BLING III study: a phase 3 multicentre randomised controlled trial of continuous versus intermittent β -lactam antibiotic infusion in critically ill patients with sepsis. Crit Care Resusc 2021;23:273-84.