

## 2024 Pharmacy to Dose Research Article of the Year Nominees

### 1. Atypical Coverage in ICU CAP

- a. Alexandra Greco Kinney, PharmD, BCCCP
- b. **Greco Kinney A**, Kovacic Scherrer N, Sarkar S, Jain P, Wen S, Hadique S.  $\beta$ -Lactams plus doxycycline versus azithromycin for treatment of severe community-acquired pneumonia in critically ill patients. *J Antimicrob Chemother*. 2023 Dec 1;78(12):2816-2823. <https://pubmed.ncbi.nlm.nih.gov/37814829/>

#### Why Should This Study Be Considered?

- c. This project idea was formulated during a topic discussion when a gap in the literature was recognized and we wanted to study it. Further, the protocol at WVU Medicine was to utilize doxycycline to cover atypical organisms in community acquired pneumonia, despite the lack of data. Both medical ICU teams used doxycycline and azithromycin, based on attending preference, so the research team knew this idea would be feasible. The investigators built an alert system through their In-Basket messaging on Epic to alert them when beta lactams + either doxycycline or azithromycin were ordered on a patient. The investigators would then screen the patient for inclusion/exclusion; if included in the study, they would then data collect. Because of the exclusion (mainly of patients having COVID), this study took ~4 years and ~800 patients reviewed to reach the goal study population.

It was very rewarding to have 4 years of work finally published (perseverance at its finest). The findings were also presented the findings to our hospital's Antimicrobial Stewardship Committee where it was well received, and they are interested in a study that may help identify possible factors that make patients more at risk for atypical organisms as they do not think atypical coverage is even indicated in all patients with CAP.

### 2. BLING III

- a. Jason Roberts, BPharm, PhD, FSHP
- b. Dulhunty JM, Brett SJ, De Waele JJ, Rajbhandari D, Billot L, Cotta MO, Davis JS, Finfer S, Hammond NE, Knowles S, Liu X, McGuinness S, Mysore J, Paterson DL, Peake S, Rhodes A, **Roberts JA**, Roger C, Shirwadkar C, Starr T, Taylor C, Myburgh JA, Lipman J; BLING III Study Investigators. Continuous vs Intermittent  $\beta$ -Lactam Antibiotic Infusions in Critically Ill Patients With Sepsis: The BLING III Randomized Clinical Trial. *JAMA*. 2024 Aug 27;332(8):629-637. <https://pubmed.ncbi.nlm.nih.gov/38864155/>

### Why Should This Study Be Considered?

c. THE BLING research program was a Royal Brisbane and Women's Hospital and University of Queensland-led research program aiming to measure the clinical benefit of administering beta-lactam antibiotics by continuous infusion versus the standard short 30-min infusions multiple times per day in critically ill adult patients with sepsis. A series of in vitro and clinical dosing studies have confirmed that administering these antibiotics, the most common used in sepsis, 'should' result in better bacterial killing.

The final study BLING III (sponsored by The George Institute for Global Health) enrolled >7000 patients from 104 intensive care units in 7 countries and found that beta-lactam administration as a continuous infusion was associated with an 1.8% absolute reduction in patient death at 90-days after study enrolment. Although this did not meet statistical significance, the pre-specified adjusted analysis (accounted for covariates like drug, age, sex and sickness severity, a statistically significant 2.2% reduction in mortality was observed. Clinical cure was also significantly better in the continuous infusion group. In a co-published systematic review and meta-analysis, improved clinical cure and 90-day mortality was also significant and in fact found that 26 patients need to be treated with continuous infusion to save one life that would not have otherwise survived with current standard care.

Administering these drugs is quite a simple intervention. In the BLING III trial there was 95% compliance with the dosing intervention. In Europe, many ICUs have been using beta-lactam continuous infusion for >10 years and find it feasible. Locally in Australia, there is mixed feedback. Some clinicians think that it is challenging occupying an intravenous line continuously given the effect it has on the need for using other lines for other intravenous medications. However, this challenge is not the experience of sites who were early adopters to this practice. Many ICUs have already changed their practice. It is reasonable to expect that the world's leading clinical practice guidelines will recommend administration of beta-lactam antibiotics by continuous infusion and so we will gradually see a global transition to this mode of administration.

This has been a partnership with many collaborators who we all now call friends. Major funding was required to be obtained from separate grant applications from Australia, New Zealand, UK and Belgium in particular. At least 3 PhD Theses were dedicated to the topic as well as Fellowships. In BLING III in particular, >130k doses of study drug, 72k hours of education, 36k health professionals, 14k loved ones providing consent, 872 site personnel, 290 contracts and >4 million data points were collected!