The Emperor’s New Clothes: Prospective Observational Evaluation of the Association between the Day 2 Vancomycin Exposure and Failure Rates among Adult Hospitalized Patients with MRSA Bloodstream Infections (PROVIDE)

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Background. Animal models of serious infection suggest that 24 hours of induced hypothermia improves circulatory and respiratory characteristics and enhances survival, but whether therapeutic mild hypothermia in such conditions is of clinical benefit remains unknown. We, therefore, tested whether reducing core temperature to 32–34°C in critically ill patients with septic shock and ventilator-demanding respiratory failure improves survival and reduces organ dysfunction. In this multi-national trial, patients with septic shock were enrolled within 6 hours of onset of septic shock and ventilator-demanding respiratory failure and randomized 1:1, stratified by site (target sample = 560), to routine thermal management or 24 hours of induced hypothermia (target 32–34°C) followed by 48 hours of normothermia. Other aspects of care were per routine in each participating center. The primary endpoint was 30-day all-cause mortality.

Results. At the third ordinary interim analysis, after recruitment of 432 participants, the Data and Safety Monitoring Board recommended the trial be terminated for futility; the conditional power for rejection of the null hypothesis in favor of efficacy was null. In the induced hypothermia group, target temperature was reached within median 3.2 hours [IQR: 2.2, 4.8], and maintained for 24 hours [IQR: 24, 24] (Figure 1). There was no evidence for a difference in 30-day mortality risk in patients randomized to hypothermia (96/217) vs. routine thermal management (77/215): relative risk 1.24 [95% CI: 0.98, 1.56] (Figure 2). At the end of the temperature intervention (72 hours), more patients assigned to hypothermia were in continued shock (vasoactive medication 71% vs. 58%; P = 0.01), and fewer cooled patients had inflammatory control (32% vs. 47% had CRP decline of >30%; P = 0.005). More harm from cooling was seen in patients entering the trial with normal renal function and with normal platelet count (P for interaction < 0.05).

Conclusion. Among patients with septic shock and ventilator-demanding respiratory failure, induced hypothermia did not improve survival, but adversely affected the duration of shock, and inflammatory control. Induced hypothermia should not routinely be used in patients with septic shock.

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BMD and ETEST were 1/1 and 1.5/1.5 mg/l, respectively. Failure occurred in 18%; 26% had AKI. Mean (SD) VαN day 18 was 18 (14) days. Mean (SD) AUC<sub>0–24</sub> was 586.9 (235.5) and 44% and 73% of patients achieved an AUC<sub>0–24</sub>/MIC<sub>₄ₐ</sub> ≥ 650 and AUC<sub>0–24</sub>/MIC<sub>₄ₐ</sub> ≥ 320. In the multivariate analyses (Figure 1), failure was not significantly different between AUC<sub>0–24</sub>/MIC<sub>₄ₐ</sub>. In contrast, AKI was significantly more common in patients with an AUC<sub>0–24</sub>/MIC<sub>₄ₐ</sub> ≥ 320. Clinicians should assess the benefits vs. risks of using VAN regimens that confer high AUC<sub>0–24</sub>/MIC exposures for patients with MRSA BSIs were not associated with better outcomes and were found to result in increased AKI. Clinicians should assess the benefits vs. risks of using VAN regimens that confer high AUC<sub>0–24</sub>/MIC exposures for patients with MRSA BSIs.

### Figure 1. Comparisons of Outcomes between AUC<sub>DAY2</sub>/MIC Exposure Groups

![Figure 1](image-url)

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### 986. Comparing the Outcomes of Adults with Enterobacteriaceae Bacteremia Receiving Short-Course vs Prolonged-Course Antibiotic Therapy

Darunee Chotiprasitsakul, MD, MPH<sup>1</sup>; Jennifer H. Han, MD, MSCE<sup>2</sup>; Anna T. Conley, BA<sup>3</sup>; Sara E. Gosgrove, MD, MS<sup>4</sup>; Anthony D. Harris, MD, MPH<sup>5</sup>; Ebbing Lautenbach, MD, MPH, MSCE, FIDSA, FSHEA<sup>6</sup>; Pranita D. Tamanna, MD, MHS<sup>7</sup>; 1Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; 2Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; 3The University of Maryland School of Medicine, Baltimore, Maryland; 4Department of Medicine, Division of Infectious Diseases, The Johns Hopkins University School of Medicine, Baltimore, Maryland; 5Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, Maryland; 6Division of Infectious Diseases, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; 7Johns Hopkins University School of Medicine, Baltimore, Maryland

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**Background.** The recommended duration of antibiotic treatment for *Enterobacteriaceae* bacteremia is between 7 and 14 days. We compared the clinical outcomes of patients receiving short-course (6–10 days) vs prolonged-course (11–15 days) antibiotic therapy for *Enterobacteriaceae* bacteremia.

**Methods.** A retrospective cohort study was conducted at The Johns Hopkins Hospital, The University of Maryland Medical Center, and The Hospital of the University of Pennsylvania including patients with monomicrobial *Enterobacteriaceae* bacteremia treated with *in vitro* active antibiotic therapy in the range of 6–15 days between January 1, 2015 and June 30, 2016 who did not receive IDC. The primary end point was 30-day mortality within 30 days after the end of antibiotic treatment for patients receiving short vs. prolonged durations of antibiotic therapy. Secondary outcomes included *Clostridium difficile* infection (CDI) and the emergence of multidrug-resistant Gram-negative (MDRGN) bacteria within 30 days after the end of antibiotic therapy.

**Results.** A total of 1,749 patients met eligibility criteria. There were 385 matched pairs who were well-balanced on baseline characteristics. The median duration of therapy in the short-course group and prolonged-course group was 8 days (interquartile range (IQR) 7–9 days) and 15 days (IQR 13–15 days), respectively. No difference in all-cause mortality between short- and prolonged-course treatment groups was observed (adjusted hazard ratio [aHR] 1.00, 95% CI 0.39–3.51). Rates of CDI were similar between the treatment groups (OR 1.17, 95% CI 0.39–3.51). There was a non-significant protective effect of short-course antibiotic therapy on the emergence of MDRGN bacteria (OR 0.59, 95% CI 0.32–1.09, P = 0.09).

**Conclusion.** Short courses of antibiotic therapy yields similar clinical outcomes to prolonged courses of antibiotic therapy for *Enterobacteriaceae* bacteremia, and may protect against subsequent MDRGN emergence.

**Disclosures.** All authors: No reported disclosures.