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L0014 Combination antibiotic therapy for methicillin-resistant *Staphylococcus aureus* bacteraemia: the CAMERA2 randomised controlled trial

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Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia is associated with worse outcomes than susceptible *S. aureus*, at least in part due to the shortcomings of vancomycin, the current standard treatment. Combination therapy with the addition of a β-lactam appears to be more effective than monotherapy in in-vitro and animal models and observational studies in humans.

Materials/methods: We conducted a multi-site, open-label randomised controlled trial across 27 sites in 4 countries (Australia, New Zealand, Singapore and Israel). Inclusion criteria were: MRSA bacteraemia within 72 hours of index blood culture draw, age ≥18 years, and likely to remain an inpatient for ≥7 days. We randomised participants to standard care (vancomycin or daptomycin) or standard care plus an anti-staphylococcal β-lactam (flucloxacillin, cloxacillin or cefazolin). The primary endpoint was a composite outcome at 90 days of: 1) all-cause mortality, 2) persistent bacteraemia at day 5 or beyond, 3) microbiological relapse, or 4) microbiological treatment failure. Secondary outcomes included individual elements of the composite primary endpoint, bacteraemia at day 2, and acute kidney injury or need for renal replacement therapy. The primary endpoint was assessed by a blinded adjudication committee. Our recruitment target was 440 patients.

Results: Of 352 participants enrolled between August 2015 to July 2018, 252 were from Australia or New Zealand, 56 from Singapore and 44 from Israel. We included 344 participants (standard care n=174, combination n=170) in the modified intention-to-treat analysis. Participants were well matched by age (median 64 years), sex (34% female), healthcare associated infection (64%), receipt of haemodialysis (15%), and Charlson comorbidity index (≥3 in 70%). At 90 days, 127 (37%) participants had reached the primary endpoint and 63 (18%) had died. The trial was stopped early on the recommendation of the data and safety monitoring board. Final complete results will be presented.

Conclusions: This investigator-initiated trial is the largest clinical trial to date of patients with MRSA bacteraemia. We demonstrate it is feasible to conduct multinational RCTs without industry funding. Such RCTs can focus on questions of common clinical practice variation with results that will influence every day clinical practice.