198. Infective Endocarditis Among Solid Organ Transplant Recipients in the United States

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Session: O-38. Transplant and Immunocompromosed Hosts

Background: With over 30,000 solid organ transplants (SOT) performed annually the United States alone, there is an urgent need to understand the risks and outcomes of infective endocarditis (IE) in SOT recipients.

Methods: We used data from the 2013–2017 Nationwide Readmissions Database (NRD). Hospitalizations associated with IE were identified using diagnosis and procedure codes. The cohort included all patients with IE, stratified by history of solid organ transplant (heart, liver, kidney, lung, intestines, pancreas). Outcomes included 60-day rates of mortality, (extracorporeal membrane oxygenation) ECMO deployment, thromboembolic events, length of stay, and inpatient costs. Regression models, weighted to account for the NRD sample design, were used to model associations between outcomes and transplant history, adjusting for patient age, sex, facility characteristics, comorbid conditions, and potential IE organism.

Results: A total of 175,682 hospitalizations associated with IE, corresponding to a national estimate of 345,236, were included. Of these, 1,299 (weighted estimate = 2,511) were associated with history of transplant. Transplant recipients were younger (54.2 vs. 59.4 years, p < 0.001), less likely to be female (33.2% vs. 40.1%), had higher rates of renal and liver disease (93.1% vs. 39.2% and 16.2% vs. 8.6%, respectively, p < 0.001 for both). The most common SOT organ (allowing for multiple organs) was kidney (75%) followed by liver (11.5%) and heart (10.5%). Compared to non-SOT patients with IE, SOT recipients with IE were associated with lower risk of mortality [adjusted relative risk (aRR): 0.74, 95% confidence interval (CI) (0.61, 0.89)], lower risk of prolonged mechanical ventilation [aRR 0.80 (0.68, 0.93)], 2.2 fewer inpatient days (-3.5 to -0.8) and $7,000 lower charges (-$9,700, -$4,300), after adjustment.

Table: 60-Day Outcomes, Stratified by SOT History

	No N=174,383 (%) [Weighted N = 342,725]	Yes N=1,299 (%) [Weighted N = 2,511]	Unadjusted Relative Risk (95% CI)	Adjusted Relative Risk (95% CI)
Mortality	42,119 (12.3)	224 (8.9)	0.73 (0.60, 0.88)	0.74 (0.61, 0.89)
Prolonged Mechanical Ventilation	53,804 (15.7)	295 (11.7)	0.77 (0.66, 0.90)	0.80 (0.68, 0.93)
ECMO Deployment	1,021 (0.3)	*	0.64 (0.16, 2.67)	0.57 (0.13, 2.47)
Thromboembolic Event	74,302 (21.7)	294 (11.7)	0.56 (0.47, 0.67)	0.85 (0.72, 1.00)
			Unadjusted Incremental Difference** (95% CI)	Adjusted Incremental Difference (95% CI)
Length of Stay (Days)	15.2 (17.5)	12.8 (17.9)	-2.4 (-3.7, -1.0)	-2.2 (-3.5, -0.8)
Total Inpatient Cost ($1000s)	42.9 (62.8)	36.3 (52.5)	-6.7 (-9.8, -3.3)	-7.0 (-9.7, -4.3)

* N < 10; result cannot be displayed due to data use restrictions
** Incremental Difference is expressed as average among SOT-related admissions minus average among non-SOT-related admissions

Conclusion: IE complicated by SOT history was associated with paradoxically better outcomes than IE in patients without SOT history. The selection process underlying receipt of transplant may partially explain these differences in outcomes.

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199. Short versus Extended Antibiotic Treatment with a Carbapenem for High-risk Febrile Neutropenia in Hematology Patients with Fever of Unknown Origin: A Randomized Multicenter Noninferiority Trial

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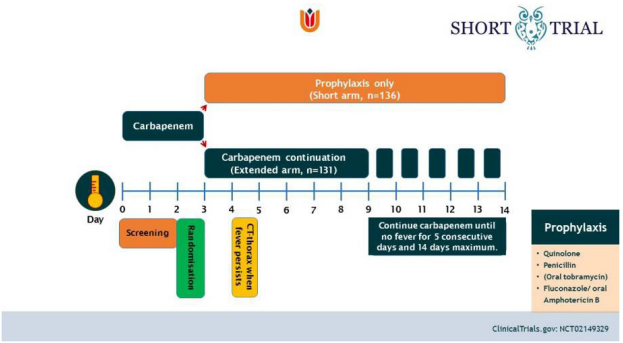
Session: O-38. Transplant and Immunocompromosed Hosts

Background: In hematology patients with high risk neutropenia due to intensive chemotherapy the optimal antibiotic treatment duration for fever of unknown origin (FUO) is unknown. Early antibiotic discontinuation has been advocated to reduce unnecessary exposure to broad-spectrum antibiotics, but there is limited evidence for the safety of this strategy. We aimed to assess if short treatment with carbapenems is non-inferior to extended treatment for neutropenic patients with FUO.

Methods: Multicenter, open-label, randomized clinical trial in 6 centers in the Netherlands. Hematology patients with FUO during high risk neutropenia (≥7 days) were eligible for participation. Eligible patients who gave informed consent were randomly assigned (1:1) to either the short treatment arm, where the carbapenem was discontinued after 72 hours, irrespective of presence of fever, or the extended treatment arm, where the carbapenem was continued for ≥ 9 days until afebrile for 5 days or end of neutropenia (EON), whichever came first. The primary endpoint was treatment failure defined as a composite of recurrent fever or a carbapenem-sensitive infection between day 4 and day 8 and septic shock or death from day 4 until EON. Secondary endpoints included all-cause and infection-related mortality until 30 days post-EON. We used 10% as noninferiority margin.

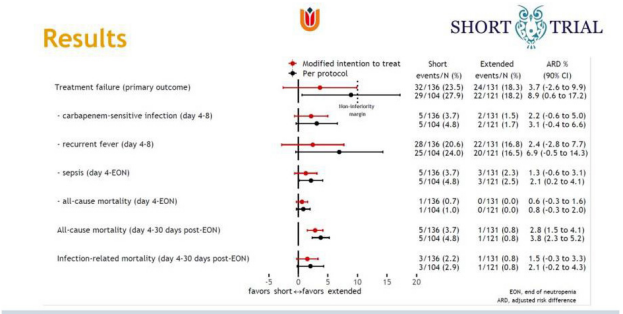
Trial Intervention Flowchart



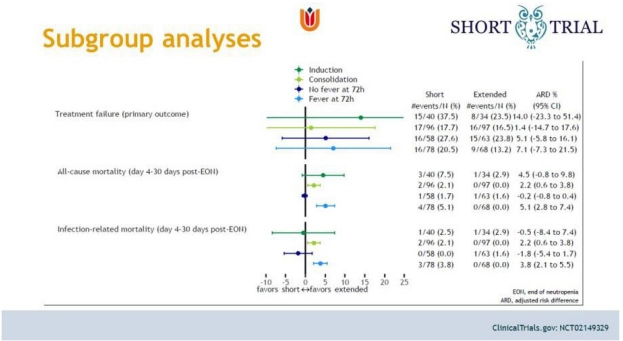
Results: Between December 2014 and August 2019 292 patients were included. Risk of treatment failure in the modified intention-to-treat analysis (mITT) was 23.5% (32/136) in the short treatment versus 18.3% (24/131) in the extended treatment arm (adjusted risk difference (ARD) 3.7% (90% CI -2.6% to 9.9%)) and in the per-protocol analysis 27.9% (29/104) versus 18.2% (22/121) (ARD 8.9% (90% CI 0.6% to 17.2%). Short treatment was non-inferior to extended treatment in the mITT population, but not in the per protocol population.

All-cause mortality until 30 days post-EON was significantly higher in the short treatment group: 3.7% (5/136) versus 0.8% (1/131) (ARD 2.8%, 95% CI 1.3 to 4.4%), but infection-related mortality until 30 days post-EON was not statistically different between the treatment arms.

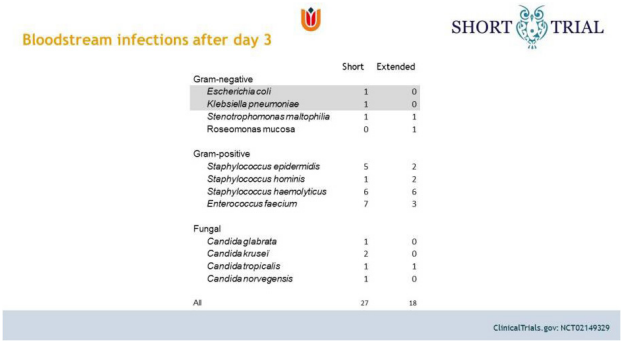
Primary and Secondary Endpoint Results



Subgroup Analyses Results

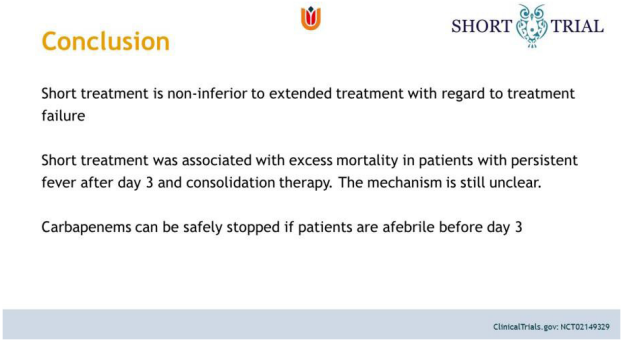


Bloodstream infections after day 3



Conclusion: Short treatment with a carbapenem in neutropenic patients with fever was noninferior to extended treatment with regard to treatment failure.

Conclusion Summary



Disclosures: **All Authors**: No reported disclosures

314. A Retrospective Review of Dalbavancin Utilization at an Academic Medical Center

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Session: P-10. Bone and Joint

Background: Dalbavancin is a novel long-acting lipoglycopeptide with increasing utilization for management of bone and joint infections as a two-dose regimen. The purpose of this study is to describe the patient characteristics, evaluate clinical outcomes, and calculate inpatient hospital days saved with use of dalbavancin as outpatient parenteral antimicrobial therapy (OPAT).

Methods: A retrospective review of patients treated with dalbavancin at University Hospital was conducted from Aug 2019- March 2020. Patients ≥ 17 yrs of age with plan to receive at least 1 dose of dalbavancin were included. All patients were initially evaluated by, and had clinic follow up with, an infectious disease physician. Information on baseline demographics, infection characteristics, treatments, and outcomes were recorded from the EMR.

Results: 42 patients met the study criteria. 62% were males with a median age of 49 yrs. 67% of patients had diabetes and 12% had a documented history of intravenous drug use. The most common indication was osteomyelitis (71%). *S. aureus* was the most commonly isolated organism in monomicrobial infections (MRSA 24%, MSSA 9.5%) and often a component of polymicrobial infections (33%). 90.5% of patients were adherent to their prescribed therapy; 1 patient missed both doses and 3 only received 1 of their recommended doses. Adverse effects were mild and noted in only 4 patients. 24 patients (57%) received concomitant antibiotics. 45% of patients achieved a cure with another 12% were classified as improved but requiring further antibiotics. 31% (N=13) had failure of therapy of which, 69% (N=9) did not achieve prior source control. 5 patients were lost to follow up. Our health system saved 160 inpatient days through dalbavancin use.

Conclusion: Dalbavancin treatment had a high adherence rate with minimal adverse effects and achieved a positive outcome in 57% of patients. Of patients that failed, the majority did not have appropriate source control. Dalbavancin use has the potential to save inpatient days while offering a more convenient option for treatment. However, further studies should be conducted to evaluate its efficacy in comparison to standard of care therapy at our institution.

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315. Alternating Magnetic Fields (AMF) and Antibiotics Eradicate Biofilm on Metal in a Synergistic Fashion

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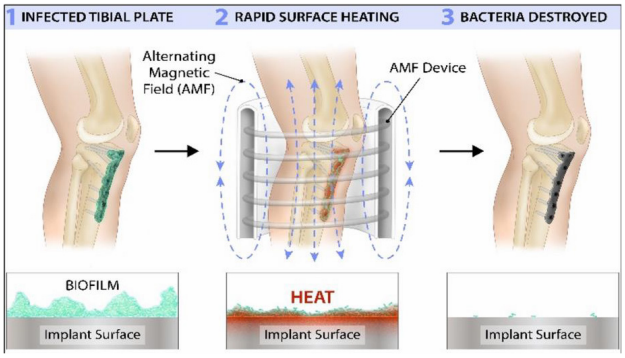
Session: P-10. Bone and Joint

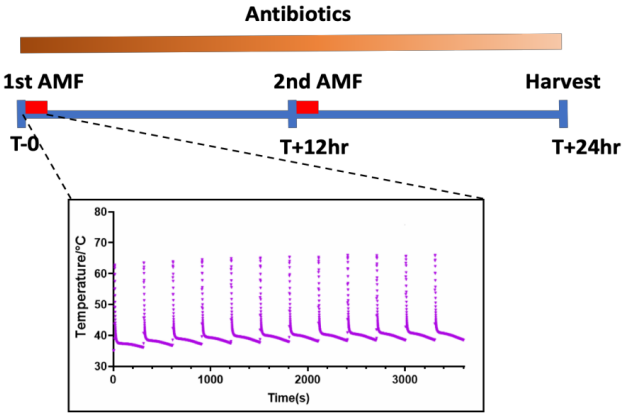
Background: Hundreds of thousands of human implant procedures require surgical revision each year due to infection. Implant infections are difficult to treat with conventional antibiotics due to the formation of biofilm on the device surface. We have developed a non-invasive method to treat metal implant infections using alternating magnetic fields (AMF). The outer surface of a metal implant is heated when exposed to AMF, and we hypothesize that this heating can be used to eradicate biofilm or sensitize them to antibiotics (Fig 1). This study investigated the interaction of biofilm and antibiotics *in vitro*.

Fig 1. Scheme showing the principle of AMF treating metal implant infection (MII).



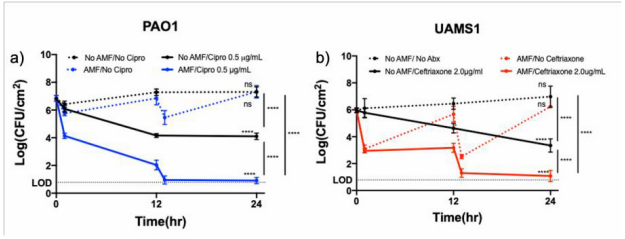
Methods: *P. aeruginosa* (PAO1) and *Staphylococcus aureus* (UAMS1) biofilms were cultured on stainless steel rings. The biofilms were then treated as in Fig 2, receiving a series of AMF exposures every 12 hours. Each dose of AMF was comprised of multiple 3s-AMF exposures every 5 min, with a peak ring temperature of 65 °C. Biofilms were incubated in the presence or absence 0.5 mg/mL ciprofloxacin or ceftriaxone. At the end of 12 and 24 hours, samples were harvested and colony forming units (CFU) were calculated.

Fig 2. AMF treatment design.



Results: AMF alone resulted in a transient decrease in CFU which recovered by the second dose. Antibiotics alone resulted in an ~2-log decrease in CFU at 24 hours. However, the combination of AMF plus cipro showed a synergistic response with a >4-log decrease (Fig 3a). Confocal microscopy confirmed these findings. This effect was not limited to *Pseudomonas aeruginosa* as similar synergistic responses were seen with *Staphylococcus aureus* and ceftriaxone (Fig 3b).

Fig 3 The bacteria number (CFU) change during 24 hr AMF and antibiotics treatment session. a) P. aeruginosa (PAO1) treated with AMF and ciprofloxacin. b) Staphylococcus aureus (UAMS1) treated with AMF and ceftriaxone.



Conclusion: When combined with antibiotics, AMF displays a synergistic effect in eradicating biofilm. This effect was seen in different pathogens and in multiple antibiotics. Synergy was seen at different target temperatures as well. This interaction has