270. Clinical Outcomes of Ceftriaxone versus Penicillin G for Complicated Viridans Group Streptococci Bacteremia

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Abstracts

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Background: Viridans group streptococci (VGS) is an infrequent yet significant cause of bloodstream infections, and complicated cases may require prolonged antibiotic therapy. Ceftriaxone (CTX) and penicillin G (PCN G) are both considered first line options for VGS infections, but comparisons between these agents are limited. We evaluated the clinical outcomes amongst patients treated with CTX and PCN G for complicated VGS bacteremia.

Methods: This was a single-center, retrospective study of adult patients with ≥1 positive VGS blood culture who were treated with either CTX or PCN G/ampicillin (both included in PCN G arm) between January 2013 and June 2019. The primary outcome was a composite of safety endpoints, including hospital readmission due to VGS or an adverse event (AE) from therapy, *Clostridioides difficile* infections, treatment modification or discontinuation due to an antibiotic-related AE, and development of extended-spectrum beta lactamase resistance. Secondary outcomes included the individual safety endpoints, VGS bacteremia recurrence, hospital readmission, and all-cause mortality.

Results: Of 328 patients screened for inclusion, 94 patients met eligibility criteria (CTX n= 64, PCN G n=34). Median age was 68 years (IQR 56–81) and 68% were male. Study patients did not present with critical illness, as reflected by a median Pitt bacteremia score of 0 in the CTX and 1 in the PCN G arms, P=0.764. *Streptococcus mitis* was the most common VGS isolate and infective endocarditis (IE) was the predominant source of infection. CTX was not significantly associated with increased risk of the primary outcome (14% vs. 27%; P= 0.139). The driver of the composite outcome was hospital readmission due to VGS bacteremia or therapy complications. Results were similar in the subgroup of patients with IE (12.5% vs. 23.5%). No secondary endpoints differed significantly between groups. On multivariate analysis, source removal was a protective factor of the primary outcome (OR 0.1; 95% CI 0.020–0.6771; P= 0.017).

Conclusion: Despite potential safety concerns with the prolonged use of CTX in complicated VGS bacteremia, this study did not demonstrate a higher rate of treatment failure, adverse events, or resistance. These findings warrant further exploration.

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271. Clinical Outcomes Treating Gram-Negative Bacteremia with Oral Beta-Lactams vs. Trimethoprim-Sulfamethoxazole or Fluoroquinolone Step-Down Therapy

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Background: Recently, studies about gram-negative bacteremia have shown that shorter courses and early step-down therapy with oral agents have equivalent outcomes compared to longer courses with intravenous therapy. The question remains, however, as to which oral agents may be most appropriate for oral conversion therapy. At Cone Health it has been common practice to de-escalate to oral beta-lactams due to local susceptibility patterns and safety concerns with fluoroquinolones. This study retrospectively evaluated the 30-day clinical outcomes of patients treated with oral beta-lactams as step-down therapy vs. fluoroquinolones and trimethoprim-sulfamethoxazole (TMP-SMX).

Methods: In this IRB approved, retrospective review, 200 patients with gram-negative rod bacteremia were screened. Sixty-seven patients were excluded due to inpatient mortality (17), transfer to another facility (7), hospice care (6), or receipt of intravenous antibiotics only (37). The most common organism isolated was *E. coli* at 57% (75/133) and a majority of cases had a genitourinary source, 79/133 (59%). The primary endpoints were 30-day readmission and mortality. Secondary endpoints included total length of antibiotic therapy and length of IV therapy.

Results: Of the 133 patients included, 101 (76%) received an oral beta-lactam and 32 (24%) received either a fluoroquinolone or TMP-SMX. In the beta-lactam group 22/101 (21.8%) were re-admitted within 30-days compared to 5/32 (15.6%) in the fluoroquinolone and TMP-SMX group (p=0.412). Each group had one patient re-admitted due to recurrence of bacteremia. The majority of patients in the beta-lactam group were re-admitted for a non-infectious reason (82%). Only 1 (1%) patient in the beta-lactam group died within 30 days of discharge compared to 2 (6%) in the fluoroquinolone group (p=0.165). Average total length of therapy in the beta-lactam group was 12.8 days compared to 14 days in the fluoroquinolone and TMP-SMX group (p=0.065). Average length of IV therapy was 3 days in the beta-lactam group and 4 days in the fluoroquinolone and TMP-SMX group (p=0.99).

Conclusion: At our institution, we have not noted any significant difference in 30-day bacteremia recurrence or mortality between those who receive oral beta-lactams or fluoroquinolones/TMP-SMX.

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272. Clinical Outcomes with Continuation of Combination Antibiotic Therapy versus De-escalation to Monotherapy for Patients with MRSA Bacteremia

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Background: Persistent methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia is associated with increased morbidity and mortality. Previous studies have demonstrated lower mortality with combination therapy (CT) compared to monotherapy (MT) for MRSA bacteremia; however, there is a lack of evidence to favor continued CT over de-escalation to MT for completion of treatment after clearance of bacteremia.

Methods: This was a single-center, retrospective study at The Ohio State University Wexner Medical Center in patients with MRSA bacteremia from November 2011 to July 2019. The primary composite outcome included inpatient infection-related mortality, 60-day readmission and 60-day bacteremia recurrence in patients receiving daptomycin and ceftaroline CT for greater than 10 days against those who received three to ten days of CT and were then de-escalated to either daptomycin, ceftaroline, or vancomycin MT. Statistical analysis used simple and multivariate logistic regression models to estimate crude and adjusted odds ratios and the 95% confidence interval to assess the relationship between the composite outcome for the MT and CT groups, while controlling for proven cofounders.

Results: A total of 286 patients with MRSA bacteremia were identified with 146 patients omitted based on exclusion criteria. The study population included 66 in the CT group and 74 in the MT group. Of those in the MT group 20 received ceftaroline, 29 received daptomycin, and 25 received vancomycin. Median age was 46 years (IQR 34.5–61), 60% required intensive care unit stay (n=84), and patients were 51% female (n=71) and 78% white (n=109). Bacteremia source was primarily intravenous drug use (40%) or line-related (16%). No significant difference was observed in the primary composite outcome (21% CT group vs 24% MT group; p=0.66). Within this outcome, there was no significant difference in readmission within 60 days (20% CT group vs 18% MT group; p=0.75), bacteremia recurrence within 60 days (3% CT group vs 7% MT group; p=0.45), or inpatient infection-related mortality (2% CT group vs 5% MT group; p=1.00).

Composite Clinical Outcome			
	CT (N = 66)	MT (N = 74)	p-value
Composite Outcome	14 (21%)	18 (24%)	0.66
Readmission Within 60 Days	13 (20%)	13 (18%)	0.75
Bacteremia Recurrence Within 60 Days	2 (3%)	5 (7%)	0.45
Inpatient Infection-Related Mortality	1 (2%)	4 (5%)	1.00

Conclusion: No significant difference was found in the composite clinical outcome for MRSA bacteremia patients with continued CT versus those who were switched to MT.

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273. Comparative Effectiveness of Ampicillin in the Treatment of Enterococcus faecalis Bloodstream Infections in Patients With Cancer

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Background: *E. faecalis* (*Efc*) isolates are usually susceptible to ampicillin (AMP). AMP-based regimens are the standard of care for enterococcal infections, although other antibiotics are often used as definitive treatment. We thus compared outcomes of patients with cancer and *Efc* bacteremia treated with AMP-containing (ACR) and non-AMP-containing antibiotic regimens (NACR).

Methods: A multicenter, prospective, observational cohort study conducted at MD Anderson Cancer Center, Henry Ford Hospital, and Memorial Hermann Health System. Eligible patients were ≥ 18 years old, diagnosed with cancer, and had at least one *Efc* bloodstream isolate collected from 12/2015 to 12/2018. Patients with polymicrobial infections were excluded. Patients were divided into two groups: i) ACR and

ii) NACR. ACR included patients who received AMP at any time during treatment; other antimicrobials were permitted. NACR patients did not receive AMP at any time. The primary outcome compared desirability of outcome ranking (DOOR) between ACR and NACR at day 14. The DOOR consisted of six hierarchical levels: 1 - death; 2 - inpatient without microbiological cure (MC) and with acute kidney injury (AKI); 3 - inpatient without MC and without AKI; 4 - inpatient admitted with MC and with AKI; 5 - inpatient with MC and without AKI; 6 - alive and discharged. Comparison of DOORs between ACR and NACR was performed using inverse probability of treatment weighted (IPTW) ordered logistic regression.

Results: Seventy-one patients were included (ACR, n = 35; NACR, n = 36). No difference was seen in DOORs at day 14 between ACR and NACR (odds ratio [OR] 1.14, 95% Confidence Interval [CI] 0.45 – 2.92, p=0.78). No difference was observed for all-cause mortality at day 14 (OR 0.6, 95% CI 0.09 – 3.77, p=0.58) or day 30 (OR 0.42, 95% CI 0.09 – 1.94, p=0.27). Patients treated with ACR received a lower median duration of other antibiotics at any point during treatment compared to NACR: daptomycin (2 v 4 days) vancomycin (2 v 4 days), and linezolid (1 v 2 days).

Conclusion: Patients with cancer and *Efc* bloodstream infections had similar outcomes when treated with ACR and NACR. ACR were associated with less use of broad-spectrum antimicrobials. Future research should focus on the ecologic impact of use of NACR.

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274. Comparison of Cefazolin Susceptibilities of Enterobacterales with an Automated Susceptibility Testing Platform versus In Vitro Antimicrobial Testing

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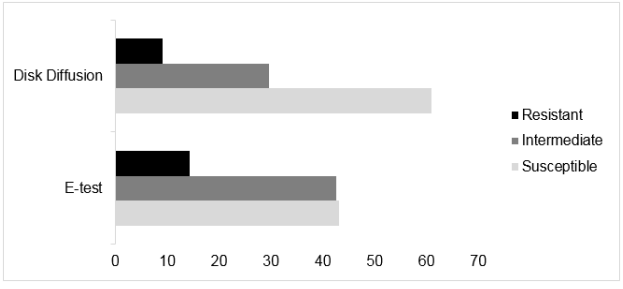
Background: The Clinical and Laboratory Standards Institute (CLSI) revised breakpoints for cefazolin (CFZ) may be difficult to implement with current automated susceptibility testing (AST) platforms and *Enterobacterales* may be falsely reported as susceptible to CFZ. The possibility remains that CFZ may then be inappropriately used as definitive therapy.

Methods: This was a retrospective observational cohort of adult patients with *Enterobacterales* bloodstream infections (BSI) reported CFZ susceptible per Vitek®2 (bioMerieux, Durham NC). The primary outcome was the percentage of CFZ susceptible *Enterobacterales* isolates using three different susceptibility testing methods: Vitek®2 automated testing, ETEST® (bioMerieux, Durham NC), and disk diffusion. Secondary outcomes included treatment failure defined as a composite outcome of 30-day all-cause inpatient mortality, 30-day recurrent BSI, 60-day recurrent infection, or infectious complications.

Results: In 195 isolates reported CFZ susceptible per Vitek®2, 84 (43.1%) were CFZ susceptible using E-test vs.119 (61%) using disk diffusion (Figure 1). Rates of treatment failure were similar in both CFZ and non-CFZ groups (33.3% vs. 38.5% respectively; p=0.57). Both groups had high rates of ID consult involvement (>60%) and source control (>80%) with urinary tract being the most reported source. No difference was noted in 30-day all-cause mortality, secondary infectious complications, 30-day readmissions, or 60-day recurrent infections. A subgroup analysis of patients receiving CFZ vs. ceftriaxone suggests treatment failure was significantly less likely to occur in the setting of source control (adjusted OR 0.06; 95% CI, 0.13–0.32) and ID consult

Figure 1: CFZ Susceptibilities by Testing Method



Conclusion: There was a large discrepancy among testing methods; additional confirmatory CFZ susceptibility testing beyond AST platforms should be considered prior to definitive use of CFZ for systemic *Enterobacterales* infections.

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275. Comparison of Cefazolin versus Nafcillin for Methicillin-Susceptible Staphylococcus aureus Bacteremia with a Deep-Seated Source

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Background: Historically, anti-staphylococcal penicillins have been the treatment of choice for methicillin-susceptible *Staphylococcus aureus* (MSSA) infections. However, cefazolin may have advantages over these agents including convenience and tolerability. Despite several studies finding similar rates of clinical efficacy using cefazolin with fewer adverse drug events, some prescribers remain hesitant to use this agent due to concern for an inoculum effect in deep-seated infections. The purpose of this study was to compare cefazolin and nafcillin for the treatment of MSSA bacteremia with exclusively deep-seated sources.

Methods: Adult patients who were admitted with MSSA bloodstream infections (BSI) treated with cefazolin or nafcillin between March 2017 and October 2019 were identified. Patients were included if their BSI had a deep-seated source, defined as endocarditis, osteomyelitis, septic arthritis, pneumonia, prosthetic material, mediastinitis, or abscess. Patients were excluded if they had polymicrobial BSI, central nervous system infection, or received less than 7 days of therapy. The primary efficacy outcome (PEO) was a composite of treatment failure, 60-day mortality, and 60-day infection relapse, and was assessed using multivariate logistic regression. The primary safety outcome (PSO) was discontinuation of therapy due to adverse drug events, which was assessed with a chi-square test.

Results: A total of 164 patients were included in this analysis (141 treated with cefazolin and 23 with nafcillin). There were no significant differences in the baseline characteristics collected (Table 1), and the most common deep-seated sources were prosthetic material and endocarditis. Treatment with nafcillin was not found to be protective against the PEO in multivariate analysis (aOR, 1.19; 95% CI, 0.42 to 3.39; $P = 0.75$), and the PSO was reached significantly more often among nafcillin recipients compared to those treated with cefazolin (7/23 [30.4%] versus 8/141 [5.7%], $P < 0.0001$).

Table 1. Characteristics of patients treated with cefazolin or nafcillin for MSSA BSI.

Characteristic	Cefazolin (n=141)	Nafcillin (n=23)	*P* value
Male, n (%)	84 (59.6)	15 (65.2)	0.608
Median age, years (IQR)	58 (21)	58 (23)	0.602
Race, %			0.133
White	61 (43.3)	13 (56.5)	
Black/African American	66 (46.8)	6 (26.1)	
Other/Unknown	14 (9.9)	4 (17.4)	
Source, %[a]			0.259
Endocarditis	37 (26.2)	11 (47.8)	
Osteomyelitis	24 (17.0)	3 (13.0)	
Pneumonia	20 (14.2)	1 (4.3)	
Abscess	22 (15.6)	3 (13.0)	
Prosthetic material	52 (36.9)	7 (30.4)	
Septic arthritis	25 (17.7)	3 (13.0)	
Mediastinitis	3 (2.1)	2 (8.7)	
Source control, n (%)	128 (90.8)	20 (86.9)	0.474
Adjunct therapy, n (%)	13 (9.2)	4 (17.4)	0.264
ID consult, n (%)	140 (99.2)	23 (100.0)	1.00

[a]Patients may have more than one source; total number of sources was 213.

Conclusion: Though the sample size was smaller than desired, cefazolin and nafcillin appeared to have similar efficacy for the treatment of MSSA BSIs with deep-seated sources. Nafcillin was associated with significantly more adverse drug events leading to discontinuation of therapy.

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276. Comparison of Ceftaroline in Combination with Either Vancomycin or Daptomycin for the Treatment of Methicillin-resistant Staphylococcus aureus Bacteremia

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Background: Recent studies have suggested that combination therapy may be preferred to monotherapy for select patients with methicillin-resistant *Staphylococcus aureus* bacteremia (MRSA-B); however, direct comparison between various combination regimens is lacking.

Methods: This was a multicenter, retrospective cohort study evaluating adult patients with MRSA-B who received vancomycin/ceftaroline (VAN+CPT) or daptomycin/ceftaroline (DAP+CPT) for at least 48 hours between April 1, 2017 and June 30, 2019. Patients with primary respiratory or central nervous system infections were excluded. The primary endpoint was rate of clinical success, defined as survival at 90 days, sterilization of blood cultures within 96 hours of combination therapy initiation, no perceived clinical failure requiring a change in MRSA-active therapy, and absence of recurrence. Secondary endpoints included time to culture clearance from combination therapy initiation, 30-day and in-hospital mortality, adverse events prompting antibiotic discontinuation, and hospital and intensive care unit length of stay.

Results: A total of 54 patients were included in the VAN+CPT group and 25 patients in the DAP+CPT group. Baseline characteristics were generally similar