Table 3. Infection groups depending on the presence or not of resistance.

| | MRSA, n (%) 211 | MSSA, n (%) 340 | Diff (95%CI)** |
|---|---|---|---|
| ***Skin and soft tissues*** | 137 (65%) | 219 (64%) | 1 (-9, 8) % |
| Blood cultures done | 25 (18%) | 52 (24%) | -6 (-15, 3) % |
| **Positive blood cultures** | **6 (24%)*** | **25 (48%)*** | **-24 (-46, -2) %** |
| Treatment | | | |
| Surgical treatment only | 61 (46%) | 89 (42%) | 4 (-7, 15) % |
| Spontaneous drainage only | 60 (45%) | 86 (40%) | 5 (-6, 16) % |
| Surgical & spontaneous drainage | 4 (3%) | 9 (4%) | -1 (-5, 3) % |
| **No drainage** | **9 (7%)** | **29 (14%)** | **-7 (-13, -1) %** |
| *missing* | 3 | 6 | |
| Localization | | | |
| **Face, head, and neck** | **28 (21%)** | **71 (33%)** | **-12 (-21, -3) %** |
| Upper limbs | 25 (19%) | 45 (21%) | -2 (-11, 5) % |
| **Lower limbs** | **51 (38%)** | **57 (26%)** | **12 (2, 22) %** |
| Chest | 17 (13%) | 23 (11%) | 2 (-5, 9) % |
| Abdomen | 4 (3%) | 8 (4%) | -1 (-5, 3) % |
| Hip | 6 (4%) | 7 (3%) | 1 (-3, 5) % |
| Genitalia | 3 (2%) | 7 (3%) | -1 (-4, 2) % |
| *missing* | 2 | 3 | |
| ICU admission | 7 (4%) | 8 (5%) | -1 (-5, 3) % |
| Mechanical ventilation | 5 (4%) | 3 (1%) | 3% (-1, 7) % |
| Vasoactive support | 5 (4%) | 5 (2%) | 2% (-2, 6) % |
| ***Bacteremia*** | 56 (27%) | 103 (30%) | -3 (-11,4) % |
| Origin | | | |
| Health care-associated infection | 8 (14%) | 22 (21%) | -7 (-20, 5) % |
| Community-onset infection | 46 (85%) | 76 (78%) | 7 (-6, 20) % |
| *missing* | 2 | 5 | - |
| Type | | | |
| Primary | 4 (7%) | 17 (17%) | -10 (-20, 0) % |
| Secondary | 52 (93%) | 86 (84%) | 9 (-1,19) % |
| Secondary infection | | | |
| **Osteoarticular** | **38 (73%)*** | **46 (53%)*** | **20 (4, 36) %** |
| Pulmonary | 9 (17%)* | 10 (12%)* | 5 (-7, 17) % |
| **Skin and soft tissue (SSTI)** | **3 (6%)*** | **18 (21%)*** | **-15% (-26, -4) %** |
| **Others** | **2 (4%)*** | **12 (14%)*** | **-10 (-19, -1) %** |
| Symptoms | | | |
| Fever | 48 (86%) | 81 (79%) | 7 (-5, 19) % |
| Upper respiratory tract symptoms | 11 (20%) | 18 (17%) | 3 (-10, 16) % |
| Lower respiratory tract symptoms | 10 (18%) | 12 (12%) | 6 (-6, 18) % |
| ***Limb pain and impairment*** | 36 (67%) | 43 (43%) | 24% (8, 40) % |
| Emesis | 9 (17%) | 19 (20%) | -3 (-16, 9) % |
| Abdominal pain | 7 (13%) | 15 (14%) | -1 (-12, 10) % |
| Skin injury or lesion | 8 (14%) | 16 (16%) | -2 (-14, 10) % |
| **PICU admission** | **29 (52%)** | **29 (28%)** | **24 (8, 40) %** |
| **Mechanical ventilation** | **17 (30%)** | **13 (13%)** | **17 (3, 31) %** |
| **Vasoactive support** | **21 (38%)** | **18 (17%)** | **21 (6, 36) %** |

Table 3b. Infection groups depending on the presence or not of resistance

| | | | |
|---|---|---|---|
| ***Osteoarticular*** | 59 (43%) | 77 (56%) | 5 (-3, 13) % |
| Diagnostic | | | |
| Osteomyelitis (OM) | 24 (41%) | 36 (43%) | -2 (-19,15) % |
| Septic arthritis (SA) | 18 (31%) | 27 (33%) | -2 (-18, 14) % |
| Both (SA & OM) | 16 (27%) | 13 (16%) | 11 (-3, 25) % |
| History | | | |
| Local inflammatory data | 42 (74%) | 51 (73%) | 1 (-14, 16) % |
| *missing* | 2 | 7 | |
| Fever (14 days) | 6 (11%) | 8 (11%) | 0 (-11, 11) % |
| *missing* | 3 | 3 | |
| Trauma in area (14 days) | 24 (44%) | 23 (34%) | 10 (-7, 27) % |
| *missing* | 4 | 9 | |
| Localization | | | |
| Face, head, and neck | 0 (0%) | 1 (1%) | -1 (-3, 1) % |
| Upper limbs | 7 (12%) | 10 (13%) | -1 (-12, 10) % |
| Lower limbs | 43 (75%) | 52 (69%) | 6 (-9, 21) % |
| Chest | 1 (1%) | 0 (0%) | 1 (-2, 4) % |
| Hip | 7 (12%) | 13 (17%) | -5 (-17, 7) % |
| *missing* | 2 | 2 | |
| **ICU admission** | **21 (36%)** | **9 (12%)** | **24 (10, 38) %** |
| **Mechanical ventilation** | **11 (19%)** | **2 (3%)** | **16 (5, 27) %** |
| **Vasoactive support** | **16 (27%)** | **4 (5%)** | **22 (10, 34) %** |
| Surgical treatment | 55 (93%) | 70 (91%) | 2 (-7, 11) % |
| **More than 1 surgical procedure*** | **49 (89%)*** | **43 (61%)*** | **28 (14, 42) %** |
| **More than 3 surgical procedures*** | **25 (45%)*** | **17 (24%)*** | **21 (4, 38) %** |
| ***Pneumonia*** | 23 (11%) | 22 (6%) | 5 (0, 10) % |
| Chest X-ray | | | |
| **Interstitial and alveolar pattern** | **1 (4%)** | **8 (38%)** | **-34 (-56, -12) %** |
| **Lobar and multi-lobar consolidation** | **22 (96%)** | **13 (62%)** | **34 (12, 56) %** |
| Complicated pneumonia*** | **13 (57%)** | **5 (24%)** | **33 (6,60) %** |
| *missing* | 0 | 1 | |
| Surgical treatment**** | | | |
| thoracentesis | 0 (0%) | 1 (4%) | -4 (-12, 4) % |
| thoracostomy | 6 (23%) | 5 (23%) | 0 (-25, 25) % |
| thoracoscopic | 5 (22%) | 3 (14%) | 8 (-14, 30) % |
| thoracotomy | 3 (9%) | 0 (0%) | 9 (-3, 21) % |
| lobectomy | 1 (4%) | 0 (0%) | 4 (-4, 12) % |
| **ICU admission** | **17 (74%)** | **11 (50%)** | **24 (-3, 52) %** |
| **Mechanical ventilation** | **14 (61%)** | **7 (32%)** | **29 (1, 57) %** |
| **Vasoactive support** | **12 (52%)** | **6 (27%)** | **25 (-3, 53) %** |

MSSA: Methicillin-susceptible Staphylococcus aureus; MRSA: Methicillin-resistant Staphylococcus aureus. HAI: Health care-associated infections.
*percentage out of the blood cultures, secondary bacteremia or surgical treatment.
**Differences and 95% confidence intervals calculated as the percentage with MRSA minus the percentage with MSSA. Negative values represent a higher proportion of patients with MSSA for the given variable.
*** Complicated pneumonia defined as the presence of empyema, pneumatoceles, pleural effusion, necrotizing pneumonia, or cavitation.
****Each case could require more than one type of procedure.

***Conclusion.*** MRSA was associated with more severe course in bacteremia, OI and pneumonia. It is interesting that some classically risk factors associated with MRSA infections were found to be related to MSSA. In general, with SSTI exception, MRSA increase risk of PICU, mechanical support and inotropic support in a pediatric population in Bogotá, Colombia.

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## 1143. Safety and Efficacy of Ceftolozane/Tazobactam Versus Meropenem in Neonatal and Pediatric Participants With Complicated Urinary Tract Infection, Including Pyelonephritis: A Phase 2, Randomized, Clinical Trial

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**Session:** P-64. Pediatric Bacterial Studies (natural history and therapeutic)

***Background.*** Ceftolozane/tazobactam (C/T) is a cephalosporin–β-lactamase inhibitor combination approved to treat complicated urinary tract infections (cUTI), complicated intra-abdominal infections, and nosocomial pneumonia in adults. Safety and efficacy of C/T in neonatal and pediatric participants with cUTI was assessed.

***Methods.*** This phase 2, randomized, double-blind study (NCT03230838) compared C/T with meropenem (MEM) for treatment of cUTI, including pyelonephritis in participants from birth to 18 years of age. Treatment duration was 7-14 days. After 3 days of intravenous therapy, optional oral step-down therapy was allowed. Participants were stratified and dosed by age group (Table 1). The primary objective was to evaluate the safety and tolerability of C/T compared with MEM, and key secondary end points included clinical response and per-participant microbiologic response at end of treatment (EOT) and test of cure (TOC).

**Table 1. Dosing by Age in All Participants as Treated Population**

| | C/T[a] | | MEM[a] | |
|---|---|---|---|---|
| **Age group** | **n** | **Dose** | **n** | **Dose** |
| 12 to <18 years | 15 | 1 g / 0.5 g | 5 | 20 mg/kg[b] |
| 6 to <12 years | 24 | 20 mg/kg / 10 mg/kg[c] | 8 | 20 mg/kg[b] |
| 2 to <6 years | 22 | 20 mg/kg / 10 mg/kg[c] | 7 | 20 mg/kg[b] |
| 3 months to <2 years | 24 | 20 mg/kg / 10 mg/kg[c] | 7 | 20 mg/kg[b] |
| Birth[d] to <3 months | 15 | 20 mg/kg / 10 mg/kg[e] | 6 | 20 mg/kg[b,e] |

C/T, ceftolozane/tazobactam; IV, intravenous; MEM, meropenem.

[a]Each dose of C/T or MEM was administered as a 60-minute (±10 minutes) infusion. C/T and MEM were dosed every 8 hours (±1 hour) after the previous infusion. The second IV dose had a ±4-hour window for dosing to facilitate adjustment of the IV dosing schedule (once every 8 hours) to be carried out throughout the IV dosing period.

[b]Maximum dose of MEM was 1 g per dose.

[c]Maximum dose of C/T was 1 g/0.5 g per dose.

[d]More than 32 weeks gestational age and ≥7 days postnatal.

[e]Higher MEM dosing up to 30 mg/kg every 8 hours for participants 14 days to <3 months of age permitted at the investigator's discretion.

***Results.*** Participants were randomized 3:1 and treated with C/T (n=100) or MEM (n=33). The microbiologic modified intent-to-treat population (mMITT) included 95 participants in the C/T (n=71) and MEM (n=24) arms; the most common reason for mMITT exclusion was lack of a qualifying baseline uropathogen (28.4%). Pyelonephritis was the most common baseline diagnosis (83.2%), and Escherichia coli was the most common qualifying baseline uropathogen (77.9%). Overall mean treatment duration was comparable in both arms (C/T, 10.2 days; MEM, 10.7); a total of 50 (70.4%) and 20 (83.3%) participants switched to optional oral step-down therapy in the C/T and MEM arms, respectively, both for a mean of approximately 6 days. The overall incidence of adverse events (AE; all and drug related), serious AE (SAE), and AE leading to discontinuation was comparable between C/T and MEM arms. There were no AE leading to death, drug-related SAE, or discontinuations due to drug-related AE or SAE (Table 2). For C/T and MEM, rates of clinical cure and microbiologic eradication at EOT and TOC were high (Figure).

**Table 2. Adverse Events (All Participants as Treated Population)**

| | C/T (N=100) | MEM (N=33) | Difference[a,b] (95% CI) |
|---|---|---|---|
| Participants with, n (%) | | | |
| ≥1 AE | 59 (59.0) | 20 (60.6) | −1.6 (−19.7 to 17.9) |
| No AE | 41 (41.0) | 13 (39.4) | 1.6 (−17.9 to 19.7) |
| Drug-related[c] AE | 14 (14.0) | 5 (15.2) | −1.2 (−18.0 to 10.9) |
| Serious AE[d] | 3 (3.0) | 2 (6.1) | −3.1 (−16.9 to 3.9) |
| Serious drug-related[c] AE | 0 | 0 | 0.0 (−10.5 to 3.7) |
| Death | 0 | 0 | 0.0 (−10.5 to 3.7) |
| Discontinued due to AE[e] | 1 (1.0) | 0 | 1.0 (−9.5 to 5.5) |
| Discontinued due to drug-related[c] AE | 0 | 0 | 0.0 (−10.5 to 3.7) |
| Discontinued due to serious AE | 0 | 0 | 0.0 (−10.5 to 3.7) |

AE, adverse event; C/T, ceftolozane/tazobactam; MEM, meropenem.

[a]Difference in C/T minus MEM.

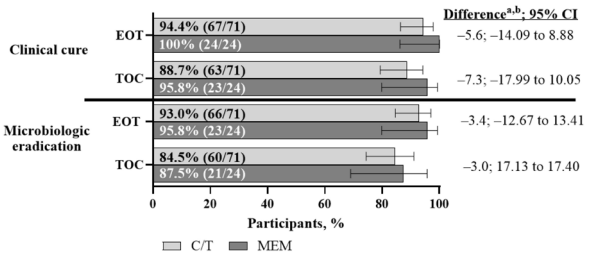
[b]Based on Miettinen & Nurminen method.

[c]Determined by the investigator to be related to the study drug.

[d]Serious AE in the C/T arm were acute pyelonephritis, pyelonephritis, and upper respiratory tract infection (1 participant each); in the MEM arm, the serious AE were hypertension and pyrexia.

[e]One participant in the C/T arm had an AE leading to discontinuation of study treatment, which also met the protocol-defined discontinuation criterion for participants on intravenous study treatment who have creatinine clearance <50 mL/min/1.73 $m^2$. The participant discontinued due to chronic kidney disease, which was not considered by the investigator to be drug related and resolved.

**Figure. Clinical and Microbiologic Response at EOT and TOC (mMITT Population)**




C/T, ceftolozane/tazobactam; EOT, end of treatment; MEM, meropenem; mMITT, microbiologic modified intent-to-treat; TOC, test of cure.

[a]Difference in C/T minus MEM.

[b]The percent difference was based on the Miettinen & Nurminen method stratified by age group with Cochran-Mantel-Haenszel weights. If there was a zero count in any class of the stratum, the groups with the lower count were pooled with the near age group stratum in the model.

***Conclusion.*** In this study, C/T was well tolerated with a safety profile comparable to MEM and to the previously reported safety profile for C/T in adults with cUTI. C/T achieved high clinical cure and microbiologic eradication rates and is a potential new treatment option for children with cUTI.

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## 1144. Evaluation of Procalcitnonin Usage in Neonates Presenting with Fever or Suspected Sepsis

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**Session:** P-64. Pediatric Bacterial Studies (natural history and therapeutic)

***Background.*** Clinical evaluation alone is not effective in identifying serious bacterial infections (SBI) in neonates presenting with suspected sepsis and fever. A clinical decision making tool to aide in evaluating neonates presenting to the pediatric emergency department (PED) uses urinalysis, absolute neutrophil count (ANC), and procalcitonin (PCT) and together has high negative predictive value (NPV) for SBI. Use may decrease invasive testing, antibiotic exposure, and rates of admission. The tool was incorporated into hospital guidelines in October 2020. The purpose is to assess implementation and prediction of SBIs.

***Methods.*** This is a single-center quality improvement study at an academic medical center. Neonates less than 60 days presenting with fever or suspected sepsis were included in the baseline group from October 2019- March 2020 or the post-implementation group from October 2020- March 2021. Exclusion criteria were receiving antibiotics 48 hours before PED visit, pre-existing medical conditions, indwelling devices, soft-tissue infections, and ≤ 36 weeks gestation. Implementation and guideline compliance was assessed in neonates aged 29-60 days as the primary outcome. Secondary endpoints include initiation of empiric antibiotics, rates of admission, rates of re-presentation within 30 days, and rates of lumbar punctures in all included patients.

***Results.*** The baseline group had 29 patients and the post-implementation group had 35 patients who met inclusion/exclusion criteria. Baseline characteristics were similar with higher SBI rates in the post-implementation group having 8 SBIs while the baseline group had 4. There were 16 patients aged 29-60 days in the baseline (55%) and 17 in the post-implementation groups (49%). Complete labs were available for 9 patients (53%) and guideline compliance was 89%. NPV in neonates aged 0-60 days with negative urinalysis, ANC, and PCT was 100%. Rates of secondary endpoints were slightly higher in the post-implementation group along with higher rates of infections.

***Conclusion.*** High NPV in this small cohort is an indication for continued use of this tool in neonates presenting to the PED with suspected sepsis or fever. Further education to increase use and expansion to all neonates should be considered based on overall NPV and previous studies.

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## 1145. The Role of the Plasmid-Mediated Fluoroquinolone-Resistance (PMFQR) Genes As Resistance Mechanisms in Pediatric Infections due to Enterobacterales (Ent)

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**Session:** P-64. Pediatric Bacterial Studies (natural history and therapeutic)

***Background.*** Fluoroquinolones (FQs) are not commonly prescribed in children, yet the increasing incidence of multidrug resistant (MDR) Ent infections in this population often reveals FQ resistance. We sought to define the role of FQ resistance in the epidemiology of MDR Ent in children, with an overall goal to devise treatment and prevention strategies.

***Methods.*** A case-control study of children (0-18 years) at 3 Chicago hospitals was performed. Cases had infections by FQ susceptible, 3rd generation cephalosporin-resistant (3GCR) and/or carbapenem-resistant (CR) Ent harboring a non or low level expressed PMFQR gene (PMFQS Ent). Controls had FQR infections due to 3GCR and/or CR Ent with expressed PMFQR genes (PMFQR Ent). We sought *bla* genes by PCR or DNA (BD Max Check-Points assay®) and PMFQR genes by PCR. We performed Rep-PCR, MLST, and *E. coli* phylogenetic grouping. Demographics; comorbidities; and device, antibiotic, and healthcare exposures were evaluated. Predictors of infection were assessed.

***Results.*** Of 170 G3CR and/or CR Ent isolates, 85 (50%) were FQS; 23 (27%) had PMFQR genes (PMFQS cases). 85 (50%) were FQR; 53 (62%) had PMFQR genes (PMFQR controls). The median age for children with PMFQS Ent and PMFQR Ent were 4.3 and 6.2 years, respectively (p=NS). Of 23 PMFQS Ent, 53% were *Klebsiella* and of 53 PMFQR Ent, 76% were *E. coli*. The most common *bla* and PMFQR genes in PMFQS Ent were $bla_{\text{SHV ESBL}}$ (44%); *oqxB* (57%) and *aac-6'1b-cr* (52%) and in PMFQR Ent were $bla_{\text{CTX-M-1 group}}$ (76%); *aac-6'1b-cr* (91%) and *oqxA* (17%).

Multivariable regression analysis showed children with PMFQS Ent infections were more likely to have hospital onset infection (OR 5.7, 95% CI 1.6-22) and isolates with multiple *bla* genes (OR 3.8, 95% CI 1.1-14.5). The presence of invasive devices mediated the effects of healthcare setting in the final model. Differences in demographics, comorbidities, or antibiotic use were not found.

***Conclusion.*** Paradoxically, PMFQS Ent infections were often hospital onset and PMFQR Ent infections were community onset. PMFQS Ent commonly co-harbored multiple *bla* and PMFQR genes, affecting therapeutic options and suggesting need for contact precautions. Control of PMFQS *Ent* infections in children will require validating sources and risk factors.

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