2275. Novel Therapeutic Options for the Treatment of Multi-Drug-Resistant *Achromobacter* Respiratory Infections

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Background. Respiratory infection due to *Achromobacter* species has been increasingly more common, especially in patients with cystic fibrosis (CF). Recurrent infections in these patients contribute to significant morbidity and mortality as well as lead to repeated antibiotic exposures with subsequent development of multi-drug-resistant (MDR) pathogens. Several recently approved antimicrobials target MDR Gram-negative pathogens, but none are FDA approved for MDR *Achromobacter* respiratory infections and lack susceptibility breakpoint recommendations.

Methods. This retrospective analysis evaluated hospitalized patients with MDR *Achromobacter* respiratory infections from August 2017 to March 2019 at AdventHealth Orlando, a 2,885-bed healthcare system including 8 campuses across Central Florida. The purpose of this descriptive study was to examine novel therapeutic agents for the treatment of respiratory infections due to MDR *Achromobacter*.

Results. MDR *Achromobacter* was isolated in 36 respiratory cultures from 18 unique patients. *A. xylosoxidans* (61%) and *A. denitrificans* (22%) were the most frequently isolated species. Mean patient age was 40 years, 56% were female, and 67% had CF. Treatment indications included CF exacerbation (38%), pneumonia (35%), post-lung transplant infection (16%), and other (11%). Twenty-four infections were polymicrobial (67%) and 23 infections included MDR pathogens. Minimum inhibitory concentrations (MIC) of the antibiotics used for treatment were available for 70% of cases. Of the 18 patients with isolated MDR *Achromobacter* organisms, 72% had MIC changes with 69% exhibiting higher MICs on subsequent testing. Novel agents were used in 63% of cases (Table 1) for an average duration of 10 days. Eravacycline was the most frequently used monotherapy agent (5/6 cases) and the most utilized novel antibiotic (21%). All-cause readmission rates at 30 days was 33%; 92% was due to infection. Inpatient all-cause mortality was 11%.

Conclusion. Antibiotics available to treat MDR *Achromobacter* infections are limited and lack standard susceptibility breakpoint recommendations. Based on this evaluation, novel agents, such as eravacycline or meropenem/vaborbactam, may be viable treatment options for patients with MDR *Achromobacter* respiratory infections.

Table 1: Novel Antibiotics Used in the Treatment of MDR Achromobacter

Drug	# of Treatment regimens	Mean Days of Therapy	Lowest MIC (mcg/mL)	Mean MIC (mcg/mL)	Highest MIC (mcg/mL)
Eravacycline	13	8.6	1	2	2
Meropenem/vaborbactam	9	9.1	0.25	50	256
Ceftolozane/tazobactam	4	8.3	12	211	256
Ceftazidime/ avibactam	3	16.7	2	8	16
Cefidericol	2	17	S*	--	--

*Based on CLSI 2019 disk diffusion breakpoints for *P. aeruginosa* (≤4 = Susceptible, 8 = Intermediate, ≥16 = Resistant)

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

2276. Clinical Epidemiology of the Carbapenem-Resistant *Enterobacteriaceae* (CRE) Epidemic in Colombia: A Multicenter Prospective Study

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Background. The CRE epidemic in Colombia is amplified by horizontal transmission of mobile genetic elements encoding KPC among *Enterobacteriaeae* and clonal expansion of *K. pneumoniae* clonal group (CG) 258, making the country hyperendemic for CRE. However, the clinical impact of CRE infections has not been comprehensively assessed.

Methods. In the framework of a prospective study assessing the clinical epidemiology of CRE (CRACKLE II), we report the results of the first 246 patients enrolled in 5 Colombian hospitals (from July 2017 to November 2018). Clinical variables, outcomes at 90 days post-hospitalization and susceptibility patterns were collected. Resistance to carbapenems was defined per CDC guidelines. Infection was defined with standardized criteria. All isolates which did not meet these criteria were considered colonization

Results. The majority of patients were men (66%); median age was 62 years [IQR 37–73]); 67% were admitted from home and 33% were hospital transfers. The mean Charlson Comorbidity Index and Pitt Bacteremia scores were 2 (SD = 2) and 3 (SD = 3), respectively. Most patients (60%; $n = 148$) were considered to be infected. The most frequent source of culture was urine (36%), followed by blood (30%) and wound secretions (13%). A respiratory source was found in the minority (6%) of patients. Species of CRE are summarized in Table 1 with the majority being *K. pneumoniae*. The best *in vitro* activity against CRE was found for fosfomycin (80% susceptible (47/59)), tigecycline (75% (67/89)), colistin (70% (35/50)) and amikacin (67% (148/220)). From 234 patients with available information at 90 days of follow-up, 13% were readmitted after discharge. Mortality at 30 and 90 days after a positive culture was 31% and 35%, respectively.

Conclusion. *K. pneumoniae* are the main drivers of the CRE epidemic in Colombia isolated mainly from non-respiratory sources. Non-susceptibility to last resource antibiotics (tigecycline, colistin and fosfomycin) is substantial among the Colombian isolates leaving few therapeutic options, a finding that correlates with high mortality. Our findings indicate that introduction of novel therapeutics in Colombia is urgently needed with a rampant epidemic of CRE causing high burden of disease.

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2277. Comparison of 30-day Crude Mortality Rates in Patients with Bloodstream Infections (BSIs) Caused by Colistin Susceptible-(ColS-CRKp) vs. Colistin and Carbapenem-Resistant *Klebsiella pneumoniae*(ColR-CRKp)

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Background. Colistin is a last resort antibiotic against infections with CRKp. Its increased use has led to resistance to this antibiotic.

Methods. This was a single-center, retrospective, cohort study including all CRKp BSIs treated between January 1, 2014 and July 31, 2018. Antibiotic therapy was appropriate if initiated within 5 days from the onset of BSI including at least an active drug with an adequate dosage. Exclusion criteria were missing key data, death < 24 h after inclusion, subsequent episodes in the same patients, pregnancy, polymicrobial BSI, < 18 years of age, no ID consultation, no carbapenemase gene detection by multiplex PCR for bla_{KPC}, bla_{NDM}, bla_{VIM}, bla_{IMP} and bla_{OXA48}. EUCAST breakpoints were used for antibiotic susceptibilities. Colistin MIC was determined by using broth microdilution. FDA criteria were applied for tigecycline susceptibility

Results. Among 174 CRKp BSIs, 129 met all inclusion criteria. Susceptibility to antibiotics was as follows: colistin (51.9%), tigecycline (67.4%), gentamicine (38.0%), amikacin (43.0%), meropenem (32.6%), ciprofloxacin (18.6%), TMP-SMX (24.0%), ceftazidime (7.8%), cefepime (7.8%).

66.1% and 19.4% of the patients received inappropriate therapy in ColR-CRKp and ColS-CRKp groups, respectively ($P \leq 0.001$). We incorporated interaction between colistin susceptibility and inappropriate therapy into multivariate logistic regression analysis (MLRA) that was constructed for identification of independent risk factors for 30-day mortality. The variables having $P \leq 0.1$ in crude analysis were included in MLRA. After checking correlation between variables by Pearson correlation analysis and multicollinearity analysis, the final model was builded. The results are shown in Table 2.

Conclusion. Colistin resistance and inappropriate therapy were not associated with decreased mortality individually, however their interaction significantly increased 30-day mortality rate (OR: 4.04; 95% CI: 1.62–10.02; $P = 0.003$).85.5% of ColR-CRKp isolates produced an OXA-48 enzyme which can be inhibited by ceftazidime–avibactam, but not available in our setting, treatment with this agent may have altered the mortality rates. Thus, high rate colistin resistance among CRKp isolates remains as a significant cause of mortality in our setting.

Figure 1. Results of multiplex PCR for bla $_{KPC}$, bla $_{NDM}$, bla$_{VIM}$, bla$_{IMP}$ and bla$_{OXA-48}$ genes

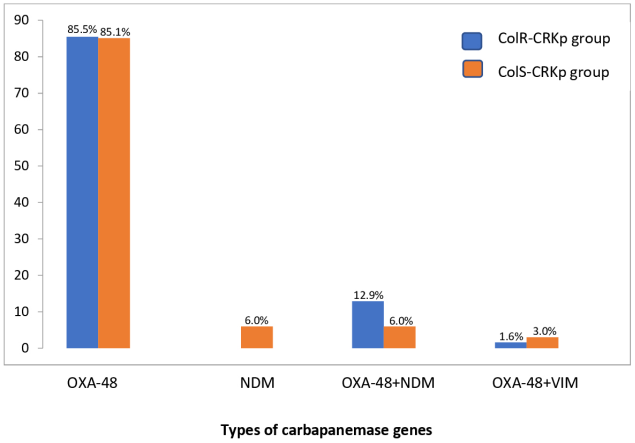


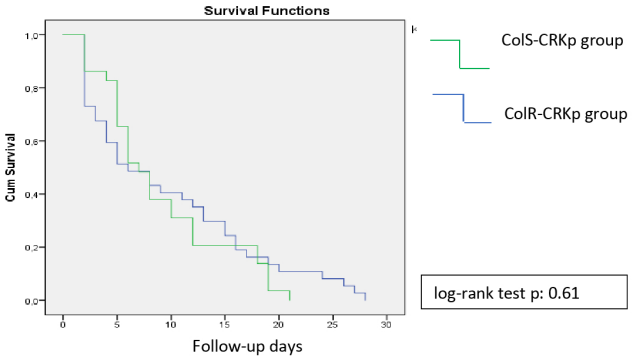
Table 1. Outcomes of patients with BSIs with CRKp according to colistin susceptibility

	ColS-CRKp (n=67)	ColR-CRKp (n=62)	Unadjusted OR (95% CI), p value	Adjusted OR (95% CI), p value
30-day crude mortality rate	29 (43.3%)	37 (59.7%)	0.51 (0.25-1.03) p=0.06	0.61 (0.19-1.98) p=0.41

Table 2. Crude analysis and multivariate analysis of factors associated with 30-day mortality rate in patients with BSIs due to ColS-CRKp and ColR-CRKp

	No. (%) of patients			Multivariate analysis	
Variable	Survivors (n=63)	Nonsurvivors (n=66)	*P* value	OR (95% CI)	*P* value
APACHE II Score (IQR)	10 (2-28)	16 (5-45)	< 0.001	Excluded	
Pitt Bacteremia Score (IQR)	2 (0-7)	5 (0-13)	< 0.001	Excluded	
INCREMENT Mortality Score (IQR)	3 (0-15)	9 (0-15)	< 0.001	**1.27 (1.14 - 1.42)**	**< 0.001**
Receiving at least one active drug in empirical therapy	29 (43%)	16 (24.2%)	0.01	Excluded	
Receiving at least one active drug in targeted therapy	50 (79.4%)	24 (60%)	0.05	Excluded	
Mechanical ventilation	14 (22.2%)	38 (57.6%)	< 0.001	Excluded	
Central venous catheter	25 (39.7%)	44 (66.7%)	0.02	Excluded	
Sepsis	18 (28.6%)	48 (72.7%)	< 0.001	Excluded	
Septic shock	6 (9.5%)	36 (54.5%)	< 0.001	Excluded	
Colistin susceptibility	38 (60.3%)	29 (43.9%)	0.06	0.65 (0.20 - 2.12)	0.47
Meropenem susceptibility	26 (41.3%)	16 (24.2%)	0.10	0.87 (0.22 - 3.45)	0.85
Amikacin Susceptibility	33 (52.4%)	22 (33.8%)	0.01	1.55 (0.38 - 6.28)	0.53
Inappropriate therapy	17 (26.9%)	37 (56.1%)	0.002	1.10 (0.25 - 4.73)	0.89
Interaction of inappropriate therapy and colistin susceptibility				**4.04 (1.62 - 10.02)**	**0.003**

Kaplan Meier Survival curves of ColS-CRKp group and ColR-CRKP group



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2278. Emergence of Resistance and Associated Mortality during Persistent *Pseudomonas aeruginosa* Bacteremia in Hematopoietic Cell Transplant Recipients and Hematologic Malignancy Patients

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Background. *Pseudomonas aeruginosa* (PSA) bacteremia causes significant mortality in patients with hematologic malignancies (HM) and hematopoietic cell transplant (HCT) recipients in part due to intrinsic and acquired resistance mechanisms. However, the incidence of developing resistance on therapy and the associated outcomes are poorly described. We characterize the emergence of resistance on therapy and describe the outcomes of PSA bacteremia in this population.

Methods. We conducted a retrospective review of adults with HM and HCT recipients who developed PSA bacteremia between January 2012 and April 2018. A bacteremic episode was characterized as ≤ 14 days from the first positive blood culture. Persistent bacteremia was defined as a positive blood culture ≥ 72 hours of appropriate antibiotic therapy. Susceptibility testing was performed with VITEK2. Isolates were classified as "sensitive," "intermediate," or "resistant" per standard criteria; "intermediate" and "resistant" results were considered "non-susceptible."

Results. 66 episodes of PSA bacteremia occurred in 59 patients. Among episodes in which a patient survived for ≥3 days, 8 (12.1%) met criteria for persistent bacteremia. Non-susceptibility to therapy developed in 5 of 7 episodes (71.4%) of persistent bacteremia; 1 did not have susceptibilities performed on both isolates. Patients with persistent bacteremia had a second positive blood culture within a median of 3.5 days. A concomitant visceral nidus of infection (pneumonia = 6, soft tissue = 1) (P = 0.005) was identified as the primary risk factor for persistent bacteremia. Risk factors for emergence of non-susceptibility could not be determined due low number of events. Infection associated mortality (IAM) (death ≤ 14 days) occurred in 12 (17.1%) of all episodes and 6 of 8 (75%) of persistent bacteremia. Persistent bacteremia was the only risk factor associated with IAM (P = 0.0002, RR 7.3).

Conclusion. Emergence of resistance to anti-*Pseudomonal* β-lactam antibiotics frequently occurs during treatment for persistent PSA bacteremia in HCT recipients and HM patients. Persistent bacteremia is associated with a visceral nidus of infection and was the only independent predictor of IAM.

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2279. Study of Prescribing patterns and Effectiveness of Ceftolozane–tazobactam (C/T): Real-world Analysis (SPECTRA): a multi-national, multicenter observational study

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Background. C/T has demonstrated efficacy in randomized clinical trials to treat cIAI and cUTI and recently completed a study in ventilator-associated bacterial and ventilated hospital-acquired bacterial pneumonia. The purpose of this study was to evaluate the real-world clinical use and outcomes of C/T in a multi-national study.

Methods. SPECTRA is a multi-national, multicenter, retrospective, inpatient, observational study of patients treated with C/T in Australia, Austria, Germany, Italy, Spain and United Kingdom. Patients admitted with greater than 48 hours of C/T treatment were included. Demographics, clinical characteristics, treatment management patterns, microbiological findings and outcomes were analyzed.

Results. There were 155 patients from 20 participating hospitals in 6 countries. The average age was 58.0 years (±17.8) and most were male 114 (74%). The majority 130 (84%) had at least one comorbidity, with the most common being renal impairment 87 (56%), immunocompromised 62 (40%), and diabetes 52 (34%). The majority, 94 (61%), had previous hospitalizations ≥ 6 months prior to receiving C/T, of which 29 (31%) had an ICU stay and surgeries 64 (42%). Most patients 126 (82%) received antibacterials within 30 days of receiving C/T, 61 (40%) received carbapenems and 47 (31%) received aminoglycoside. The average duration of C/T was 15 (SD12) days. The source of infection was cUTI for 31 (20%), cIAI for 19 (12%) and respiratory for 43 (28%) of C/T treated patients. Most 107 (70%) had an ID consult with an average of 7 (SD 11.3) consults. The top pathogen was Pseudomonas 124 (81%) followed by E. coli 22 (14%), with 56 (37%) having a polymicrobial infection. Over half of the patients were in the ICU 84 (55%), 58 (38%) underwent at least 1 surgery, with 65 (48%) being related to the infection, 60 (39%) had sepsis and 21 (14%) had septic shock. All-cause in hospital mortality was 16%. 30-day all-cause readmission was 12% and 6% were infection related.

Conclusion. Despite the complexity of the patients in this real-world analysis, most C/T patients had beneficial outcomes that are similar to results of controlled clinical trials.

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