Methods: We obtained 33 non-duplicate isolates of MDR and XDR PA grown from blood, urine and respiratory samples collected from patients admitted between 2015 and 2019 at our two affiliate teaching hospitals. MDR PA was defined as resistance to 3 or more classes of anti-pseudomonal antibiotics, and XDR PA as resistance to all but two or less classes of anti-pseudomonal antibiotics. Antimicrobial preparations of both MP and CT were made according to manufacturer instructions. Susceptibility testing was performed using the checkerboard method in accordance to CLSI guidelines (CLSI M100, 2017). The ATCC 27853 strain of PA used as control. Synergy, additive effect, indifference and antagonism were defined as FIC (fractional inhibitory concentration) indices of ≤0.5, >0.5 to <1, >1 to <4, and >4, respectively.

Results: Thirteen (39%) of 33 PA isolates were classified as XDR, while 20 (61%) PA isolates were MDR. All isolates were resistant to MP (MIC50 >32 ug/mL), while only 2 (6%) isolates were susceptible to CT (MIC50 64 ug/mL). A synergistic effect was seen in 9 (27.3%) of PA isolates (FIC index range 0.28 to 0.5)— 2 of which were XDR PA, and 7 were MDR PA. An additive effect was seen in 12 (36.4%), with indifference seen in 12 (36.4%) of isolates. In this study, no antagonism was seen when CT and MP were combined.

Conclusion: When used in combination, CT and MP can exert a synergistic effect against MDR and XDR PA. Additive effect and indifference can also be seen when both antibiotics were used. Moreover, there was no antagonism seen when both antibiotics were combined. This study shows that the use of CT and MP in combination may be an option against XDR and MDR PA infections.

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1598. Clinical implications of azole-resistant *vs.* azole-susceptible invasive aspergillosis in hematological malignancy (CLARITY) – a multicenter study

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CLARITY study group

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Advances in the survival of patients with invasive aspergillosis (IA) are jeopardized by the emergence of azole resistance in *Aspergillus fumigatus*, which has been associated with high probability of azole treatment failure. The clinical implications of azole-resistant IA compared to azole-susceptible IA remain unclear. Thus, we seek to describe the epidemiology and to determine the efficacy of antifungal therapy in patients with documented azole-resistant IA compared to azole-susceptible IA in patients with hematological malignancy.

Methods. For proven and probable IA (EORTC/MSG 2019) caused by *A. fumigatus* in patients with hematological malignancies retrospective data were documented, comprising demographics, diagnosis, treatment, response, and outcome. Sites provided susceptibility results or respective isolates for analysis in a central laboratory.

Results. Sites in 16 countries worldwide enrolled 187 cases diagnosed with IA between 2010 and 2019; 31 (16.6%) were resistant to at least one of the clinical azoles. Fungal isolates were available from 42 cases. A mixed fungal infection was reported for 32 patients (17.1%), most were related to non-*fumigatus Aspergillus* and non-*Aspergillus* molds (n=22, 69%). Most patients were male (66.8%) and overall the majority of patients were in the age groups between 50 and 89 years (71%). Amphotericin B was used for treatment in 24 (77%) patients with azole-resistant IA, compared to 76 (49%) in the azole-susceptible group (lipid-based formulation in 98%); only five (16%) patients with azole-resistant IA were treated with an azole alone vs. 57 (36%) of those with azole-susceptible IA. Overall, all-cause mortality rate was higher for patients with azole-resistant compared to azole-susceptible IA (74.2% vs. 53.8%, log rank *P*=0.004), the 8 patients with an azole-resistant IA treated in the intensive care unit died within 1 month (**Figure 1**). Details on underlying disease and survival are given in **Table 1**.

Table 1. Underlying hematological malignancy and clinical outcome of patients with azole-resistant and azole-susceptible invasive aspergillosis

Table 1. Underlying hematological malignancy and clinical outcome of patients with azole-resistant and azole-susceptible invasive aspergillosis

	Azole-resistant IA		Azole-susceptible IA		Overall		*P*
	N	%	N	%	N	%	value
Total	31	16.6	156	83.4	187	100	
Hematologic malignancy							
Acute leukemia	13	41.9	60	38.5	73	39	0.841
Chronic leukemia	2	6.5	14	9	16	8.6	1.000
Lymphoma	4	12.9	39	25	43	23	0.167
Multiple myeloma	2	6.5	14	9	16	8.6	1.000
Other	10	32.3	29	18.6	39	20.9	0.095
Allogeneic HSCT	18	58.1	61	39.1	79	42.2	0.072
ICU stay	8	25.8	27	17.3	35	18.7	0.313
Mortality							
Overall	23	74.2	84	53.8	107	57.2	0.004
ICU	8	100	21	77.8	29	82.9	0.007

HSCT, Hematopoietic stem cell transplantation; ICU, Intensive Care Unit

P value (Fisher's Exact Test azole-resistant vs azole-susceptible IA cases; Mortality: Kaplan Meier analysis, log rank test, azole-resistant vs azole-susceptible IA cases (Overall) and ICU patients only (ICU))

Figure 1. Intensive care unit 1-year survival probability for patients with azole-resistant and azole-susceptible invasive aspergillosis

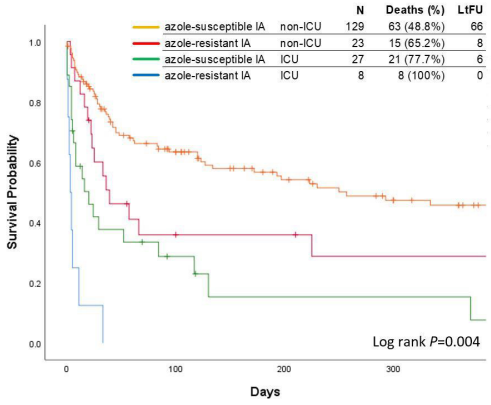

Figure 1. Intensive care unit 1-year survival probability for patients with azole-resistant and azole-susceptible invasive aspergillosis

IA, Invasive aspergillosis; ICU, Intensive care unit; LtFU, Lost to follow-up

Conclusion. Azole-resistance in IA is associated with worse outcome, especially in critically ill patients. Susceptibility testing should be considered in patients with a suspected azole-resistant IA to support treatment decisions.

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1599. Clinical Outcomes for Patients Treated with Fluoroquinolones for Bacteremia Caused by Enterobacteriaceae Reclassified as Not Susceptible by Updated CLSI Breakpoints

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Antibiotic resistance remains a pressing public health challenge. Antibiotic susceptibility testing is crucial to identify resistance and predict which antibiotics are most likely to be effective. In vitro minimum inhibitory concentrations (MICs) are interpreted using MIC breakpoints set for the United States by The Clinical and Laboratory Standards Institute (CLSI). In 2019 CLSI updated fluroquinolone (FQ) breakpoints for Enterobacteriaceae. Previously any isolate with an MIC ≤ 1 μg/mL of ciprofloxacin would be considered susceptible but based largely on pharmacokinetic/pharmacodynamic simulations the susceptibility breakpoint was revised to ≤ 0.25 μg/mL. However, the clinical relevance of this decision remains unclear.

Methods. All cases of Enterobacteriaceae bacteremia with isolates previously considered susceptible but reclassified as resistant (MIC = 1 μg/mL) in adults treated with FQs between 08/01/2018 and 07/31/2019 were identified. Demographics, clinical characteristics and outcomes were compared with an equal number of randomly selected isolates with an automated MIC reported as ≤ 0.5 μg/mL. Available stored isolates with a reported MIC of ≤ 0.5 μg/mL had manual E-testing performed to identify a more precise MIC.

Results. 29 cases with an MIC = 1 μg/mL were compared with 29 controls with a MIC of ≤ 0.5. Only 3 cases and 1 control received FQs as empiric therapy, the remaining patients in each group were transitioned to FQ after a median of 4 days of other antibiotics. No significant difference was found for predetermined outcomes including 30 day mortality, escalation after starting FQ, length of hospital stay, and readmission in 30 days (see Table). No primary outcome was thought to be related to antibiotic failure. E-testing found no isolates with an MIC = 0.5 μg/mL.

Table 1

	MIC = 1 (n = 29)	MIC ≤ 0.5 (n = 29)
30 day mortality	0	1 (3.4%)
Non-sterilization (w/FQ)	0	0
Escalation after starting FQ	1 (3.4%)	0
LOS	6.5 days	6.2 days
Readmission (30d)	6 (21%)	7 (24%)

Conclusion. Patients with Enterobacteriaceae bacteremia treated with FQs for isolates reclassified as resistant had similar outcomes to those with lower MICs. While FQs are generally not recommended as first line empiric antibiotics, FQs may still be safe to use as stepdown therapy for isolates with a ciprofloxacin MIC = 1 μg/mL, particularly if the only alternative may be IV antibiotics. A larger study is needed to confirm this.

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1600. Closing the gap on moxifloxacin breakpoints for *Stenotrophomonas maltophilia*

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Moxifloxacin (MOX) has *in vitro* activity against Enterobacterales and *Stenotrophomonas maltophilia* (SM). Although MOX commonly displays lower minimum inhibitory concentration ($MIC_{50/90}$ values against SM when compared to levofloxacin, there are currently no established MOX breakpoints for treatment of SM. The Clinical and Laboratory Standards Institute (CLSI) has established interpretive categories and MIC breakpoints for levofloxacin (S ≤2μg/ml) against SM. The US Food and Drug Administration and European Committee on Antimicrobial Susceptibility Testing provide MOX breakpoints for Enterobacterales with susceptible MICs represented at ≤ 2 μg/mL and ≤ 0.25 μg/mL, respectively. The purpose of this study was to evaluate MOX MIC distribution against SM strains recovered from clinical specimens.

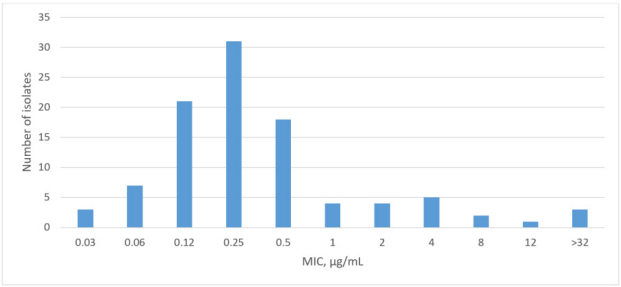
Methods. Clinical samples from patients with suspected infection during calendar year 2018 and 2019 were processed in the microbiology lab of Wake Forest Baptist Medical Center. After incubation, SM colonies were identified by MALDI-TOF system. MOX susceptibility testing was performed for these clinical isolates by gradient diffusion strip methodologies. Results were displayed as MIC (μg/mL) without interpretation. $MIC_{50/90}$ and susceptibility rates at potential breakpoints were calculated.

Results. A total of 211 isolates were tested, 112 from 2018 and 99 from 2019. MOX MIC_{50} and MIC_{90} for all isolates was 0.25 μg/mL and 2 μg/mL, respectively. The range of MIC distribution was ≤ 0.006 μg/mL to ≥ 64 μg/mL. Percent susceptibilities at incremental MICs, including established MOX breakpoints against Enterobacterales and established levofloxacin breakpoints against SM, are represented in Table 1. MIC distribution was plotted in Figure 1.

Table 1. Susceptibility rates of S. maltophilia to moxifloxacin at theoretical breakpoints

Breakpoint (μg/mL)	Percent Susceptible		
	All (n=211)	2018 (n=112)	2019 (n=99)
≤ 0.25	69%	75%	63%
≤ 1	88%	90%	85%
≤ 2	93%	97%	89%

Figure 1. Moxifloxacin MIC Distribution against All S. maltophilia Isolates



Conclusion: With no established breakpoint, these data represent one of the largest samples of MOX MICs against SM in the United States. Using the CLSI breakpoint for levofloxacin in SM (MIC of ≤2ug/ml) the overall susceptibility rate is 93%. This finding highlights the importance of performing susceptibility testing to this agent by the microbiology laboratory and the critical need for MOX breakpoints in SM.

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1601. Combination Therapy versus Monotherapy for Carbapenem-resistant Organisms: Is More Really Better?

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Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Carbapenem-resistant organisms (CROs) represent an urgent public health threat and associated with mortality rates up to 60%. Pharmacotherapy for these infections remain challenging and historically included multiple agents. Meropenem/vaborbactam and ceftazidime/avibactam are options to treat CRO infections as monotherapy; however, combination therapy is still frequently utilized. Data