1488. Relationship Between Culture Conversion and Clinical Outcomes in Patients With *Mycobacterium abscessus* (MAB) Lung Disease: A Systematic Literature Review

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Session: P-67. Respiratory Infections - Bacterial

Background. Treatment of MAB lung disease is difficult, and currently there is no consensus on the best course of treatment. We examined the relationship between culture conversion and clinical outcomes among patients with MAB lung disease.

Methods. English-language MAB lung disease studies with ≥10 patients and reporting culture conversion and/or an outcome of interest (eg, changes in symptoms, lung function, quality of life, and/or radiography) were identified from Embase, PubMed, relevant congress abstracts, and the Cochrane Library (data cutoff, September 24, 2019) using the National Institute for Health and Clinical Excellence guidance for systematic literature reviews. Two independent reviewers screened 1,551 indexed records; relevant data were extracted and are reported as population-weighted means.

Results. No study directly correlated culture conversion with a change in symptoms. In 10 studies (N=869) reporting overall symptoms and culture conversion separately, 72.5% of patients (range 36%–96%) reported symptom improvement and 56.5% (range, 13%-99%) achieved culture conversion; a weak trend between symptomatic improvement and higher culture conversion rates (R^2=0.36) was observed. Three additional studies (N=106) reported symptomatic improvement and culture conversion as a single measurement (49.6%, range, 25%-81%). Limited data indirectly correlated improvement in cough, dyspnea, hemoptysis, sputum production, and fatigue with culture conversion (1-2 studies each). Two studies directly correlated improved lung function (N=62) with culture conversion, and one study indirectly reported improved health-related quality of life (N=47) with culture conversion; no study reported radiology outcomes in relation to culture conversion.

Conclusion. This systematic literature review underscores the lack of data correlating clinical outcomes and culture conversion in patients with MAB lung disease. Limitations include a small number of studies, inconsistencies/non-reporting of methods, and poorly defined outcomes. Although indirect data indicate a weak correlation between symptom improvement and culture conversion, more evidence is needed to demonstrate a clinical outcome benefit associated with culture conversion.

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1489. Safety and Performance of a Pharmacist-Driven Nasal MRSA PCR Protocol for De-escalation of Empiric Vancomycin for Suspected Pneumonia at an Academic Medical Center

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Session: P-67. Respiratory Infections - Bacterial

Background. Limited published data supports the de-escalation of empiric anti-methicillin resistant *Staphylococcus aureus* (MRSA) antibiotics for suspected pneumonia upon negative nasal MRSA screening. Besides limited sample sizes, special populations, such as those who are immunocompromised and/or critically ill, have been underrepresented in these reports. We describe real-world efficacy and safety of a pharmacist-driven nasal MRSA PCR testing protocol implemented at Stanford Health Care in May 2018 across a diverse patient population.

Methods. This was an observational cohort study of adult patients who received vancomycin for empiric pneumonia before (PRE) vs after (POST) implementation of a pharmacist-driven nasal MRSA PCR testing protocol (between 05/01/2017 - 08/31/2017 (PRE) and 5/7/2018 - 12/31/2019 (POST). The primary outcome measure was duration of vancomycin administration. Secondary outcomes included time to vancomycin discontinuation, frequency of restarting vancomycin for empiric pneumonia within 7 days, acute kidney injury (defined as "risk" by RIFLE criteria), and MRSA respiratory cultures. Statistical methods are described in Figure A.

Figure A. Statistical methods

Statistical methods

Data were analyzed using SPSS 26.0 (IBM SPSS Statistics, IBM Corporation) software.

Categorical variables were analyzed by chi-square or Fisher's exact test when appropriate.

Continuous variables were tested for normality by use of Shapiro-Wilk test and analyzed by Student's t test or Mann-Whitney U test, where appropriate.

Categorical variables were represented by using frequencies and percentages, and continuous data are presented as the medians (interquartile ranges).

Vancomycin duration was described using Kaplan–Meier analysis. A log rank test was conducted to determine if there were differences in active vancomycin therapy distributions amongst groups.

All P values < 0.05 were considered statistically significant.

Results: Total of 610 patients were included in this study with 116 in the PRE group and 494 in the POST group. Over 40% were critically ill and approximately 37% were immunocompromised in both groups (Table 1). For the primary outcome, median vancomycin duration was significantly shorter in the POST group (1.29 days; 95% CI 1.13-1.45) vs. PRE group (1.98 days; 95% CI 1.49-2.46) ($p < 0.0005$), a 34.8% reduction (Figure 1). Median vancomycin duration was lower in patients with a negative vs positive nasal MRSA PCR (1.20 days [95% CI 1.08-1.33] vs 2.53 days [95% CI 1.77-3.29], p < 0.0005), a 52.6% reduction (Figure 2). MRSA was recovered in respiratory cultures in 1.7% vs 1.4% in the PRE vs POST groups. One (0.002%) patient had a negative nasal MRSA PCR but culture-confirmed MRSA pneumonia and recovered after completing a treatment course. Secondary safety outcomes were similar between groups (Table 2).

Tables 1 and 2: Baseline Characteristics and Secondary Outcomes

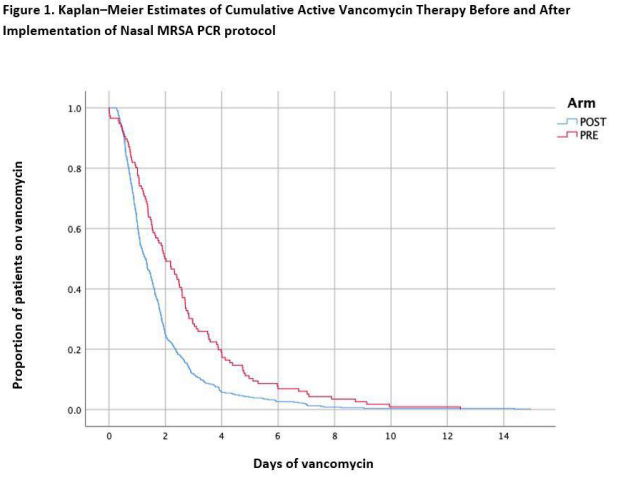
Table 1. Baseline characteristics

	Pre (n=116)	Post (n=494)	P value
Age, median (IQR), years	69 (59-78)	66 (56-76)	0.28
Sex, n (%) Male	72 (62%)	294 (60%)	0.26
Weight, median (IQR), kg	67 (57-85)	78 (64-92)	0.35
Body mass index, median (IQR), kg/m^2	23.7 (22-28)	28.5 (25-33)	0.08
Pneumonia type, n (%) CAP HAP VAP Aspiration pneumonia	 60 (52%) 12 (10%) 12 (10%) 32 (28%)	 219 (44%) 100 (20%) 43 (9%) 132 (27%)	0.09
Treatment team, n (%) BMT Hematology ICU Medicine Oncology SOT Surgery	 2 (2%) 5 (4%) 56 (48%) 32 (28%) 6 (5%) 10 (9%) 5 (4%)	 8 (2%) 24 (5%) 218 (44%) 145 (29%) 37 (7%) 35 (7%) 27 (5%)	0.94
Immunocompromised, n (%)	43 (37%)	187 (38%)	0.89

Table 2. Secondary Outcomes

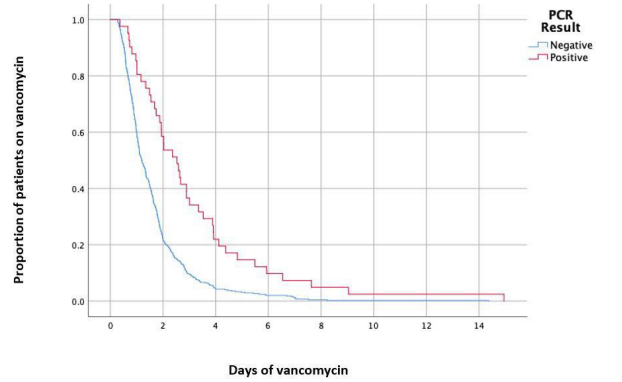
	Pre (n=116)	Post (n=494)	P value
Vancomycin restarted within 7 days for suspected pneumonia, n (%)	7 (6.0%)	31 (6.3%)	0.92
MRSA in respiratory culture	2 (1.7%)	7 (1.4%)	0.13
Hospital length of stay, days, median (IQR)	8.5 (4.3-20.5)	9.8 (4.8-19)	0.84
Acute kidney injury (RIFLE-risk), n (%)	26 (22%)	102 (21%)	0.67
Time from nasal MRSA PCR result to vancomycin discontinuation, days, median (IQR) Negative MRSA PCR Positive MRSA PCR	n/a	0.64 (0.25-1.37) 0.59 (0.22-1.28) 1.46 (0.74-3.23)	n/a
Nasal MRSA PCR turnaround time, hours, median (IQR)	n/a	5.8 (4.8-7.3)	n/a
Nasal MRSA PCR negative, n (%) Vancomycin discontinued within 24 hours	n/a	453 (92%) 317 (70%)	n/a

Figure 1. Primary Outcome: Kaplan–Meier Estimates of Cumulative Active Vancomycin Therapy Before and After Implementation of Nasal MRSA PCR protocol



Log-rank test **p <0.0005**. Median 1.29 days (95% CI 1.13-1.45) vs 1.98 days (95% CI 1.49-2.46) in POST vs PRE group

Figure 2. Secondary Outcome: Figure 2. Kaplan–Meier Estimates of Cumulative Active Vancomycin Therapy in Patients with Negative vs Positive Nasal MRSA PCR



Log-rank test **p <0.0005**. Median 1.20 days (95% CI 1.08-1.33) in POST group with negative nasal MRSA PCR vs 2.53 days (95% CI 1.77-3.29) in POST group with positive nasal MRSA PCR.

Conclusion: Pharmacist-driven nasal MRSA PCR testing is effective and safe in early de-escalation of empiric vancomycin used for pneumonia treatment in a diverse population including critically ill and immunocompromised patients.

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1490. Serious Infections Caused by Carbapenem Susceptible and Carbapenem Resistant *Acinetobacter baumannii-calcoaceticus* Complex - A Retrospective Review

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Session: P-67. Respiratory Infections - Bacterial

Background. Increasing resistance to available antibiotics, including carbapenems, is limiting effective treatment options for serious *Acinetobacter baumannii-calcoaceticus* (ABC) complex infections that are associated with high mortality. This multi-center retrospective analysis is to describe the natural history and outcomes of serious ABC infections.

Methods. This was a retrospective review of 125 cases of ABC infections from United States (US), Israel, Turkey and Russia. Baseline, microbiologic, treatment and outcomes data were collected from patients with hospital-acquired (HABP, n=23) or ventilator-associated bacterial pneumonia (VABP, n=26), bacteremia (n=36), urinary tract infections/acute pyelonephritis (n=16), and wound ABC infections (n=24) between 2017-2019.

Results. Fifty percent of cases reviewed were from the US. The median age of patients was 63 years (range 18-93), 46% were > 65 years old, 69% were male, 31% had renal failure, and 22% had septic shock. The most common co-morbidities observed were cardiac disease (41%), diabetes (32%) and moderate or severe renal disease (26%). Rates of resistance were observed as follows: ciprofloxacin 74%, ceftazidime 67%, amikacin 52% and colistin 0%. Carbapenem resistance (CR) was observed in 49% of patients. Most patients (73%) received combination therapy with 37% receiving at least 4 antibiotics. Carbapenems (40%) and penicillin/b-lactamase inhibitors (42%) were mostly used for treatment. Polymyxins were used in 18% of cases. Overall, the 28-day mortality was 34% and was highest in bacteremia (56%) and VABP (50%). CR appears to be a factor in mortality and other outcomes, as well as hospital days (table). In patients who received monotherapy, all 5 patients with CR infection died compared to 29% mortality in patients with carbapenem sensitive (CS) infection. Mortality was 70% in 20 cases when colistin was used for treatment.

Category	CR (n=60)	CS (n=63)
28-day Mortality	45%	24%
A. baumannii Eradicated	38%	56%
Clinical Cure	50%	63%
Hospital Days (mean)	16.9 d	13.7 d

Conclusion: Serious ABC infections are associated with substantial comorbidities and a high mortality rate despite treatment with combination therapy. CR appears to be a major factor in mortality. New antibiotics are urgently needed to treat serious ABC infections.

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1491. Standard- vs. High-dose Trimethoprim-Sulfamethoxazole for *Stenotrophomonas maltophilia* pneumonia

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Session: P-67. Respiratory Infections - Bacterial

Background. *Stenotrophomonas maltophilia* is a multidrug-resistant pathogen known to cause pneumonia with associated mortality rates up to 44%.[1,2] Trimethoprim-sulfamethoxazole (TMP-SMX) is the drug of choice based on available clinical evidence and excellent in-vitro susceptibility rates.3 High-dose TMP-SMX strategies recommend between 15-20mg/kg/day of the TMP component, however this has been associated with increased adverse drug events (ADE).[4,5] The optimal dosing strategy remains unclear and it is unknown whether lower doses of TMP-SMX would achieve similar outcomes.

Methods. Patients with positive respiratory cultures for *S. maltophilia* who received at least 72 hours of TMP-SMX therapy for hospital-acquired or ventilator-associated pneumonia from January 2010 to March 2020 were included. Doses were categorized as standard-dose (SD) TMP-SMX (< 15 mg/kg/day TMP) or high-dose (HD) TMP-SMX (≥ 15 mg/kg/day TMP) after adjusting for renal function. The primary outcome was clinical success, defined as the composite of resolution of signs/symptoms of pneumonia, in-hospital survival, and no escalation of care. Secondary outcomes included hospital length of stay (LOS), 30-day mortality, 30-day readmission, and ADE.

Results. Of the 44 patients meeting inclusion criteria for the study, 27 received SD and 17 received HD TMP-SMX therapy. Patients received 12 mg/kg/day (IQR 11-14) and 16 mg/kg/day (IQR 16-19) in the SD and HD groups, respectively. There was no difference in clinical success between the SD and HD group (41% vs 59%, p=0.24). Secondary outcomes were similar between both groups except for 30-day hospital readmission; the SD group had significantly lower readmission rates (6% vs 69%, p < 0.01). Rates of adverse events were not statistically different between the two groups.

Conclusion. This study provides evidence that SD TMP-SMX may achieve similar clinical efficacy to HD TMP-SMX. We found no significant difference in clinical success, LOS, 30-day mortality, or adverse events between groups. Although HD TMP-SMX is the current recommendation for *S. maltophilia* infections, concerns about tolerability and adverse effects suggest that further clinical and pharmacodynamic research is needed.

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1492. Targeted Substitution of Omadacycline in Place of Standard of Care for CABP Treatment is Associated with a Risk Reduction of Clostridioides difficile Infection and Financial Cost Savings in the Acute Care Setting

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Session: P-67. Respiratory Infections - Bacterial

Background. Real-world evidence studies indicate that around 3% of hospitalized patients with community-acquired pneumonia (CAP) develop *Clostridioides difficile* infection (CDI; Chalmers et al, *J Infect* 2016;73:45–53). Factors associated with increased CDI risk include Davis risk score (DRS) ≥ 6, and treatment with high-risk antibiotics such as fluroquinolones (FQ) and ceftriaxone (CTX). Omadacycline (OMC) is indicated for the treatment of community-acquired bacterial pneumonia (CABP) and has demonstrated a low propensity to induce CDI in preclinical and clinical studies. In the phase 3 OPTIC study, 2% of CABP patients who received moxifloxacin (MOX) developed CDI vs 0% for OMC (Stets et al, *N Engl J Med* 2019;380:517–27); 14% of MOX patients with DRS ≥ 6 developed CDI vs 0% in the OMC group (**Table 1;**