bictegravir+emtricitabine+tenofovir alafenamide (BIC+FTC+TAF) and with dolute- 
gravir and lamivudine (DTG+3TC). Here, viral breakthrough (VB) and resistance 
development were evaluated under alternating high and low drug exposures simulating 
variable adherence levels.

**Methods.** Wild-type HIV-1 (IIIB)-infected MT-2 cells were exposed to drug 
combinations and monitored for VB. Experiments alternated between high and low 
drug concentrations of either BIC+FTC+TAF or DTG+3TC (Table 1). Drug concen-
trations for each regimen were determined using human plasma-free adjusted 
clinical trough concentrations (C\text{\textsubscript{\text{tr}}}s) at simulated C\text{\textsubscript{\text{tr}}}s-2 for missing 2 or consecutives doses 
(C\text{\textsubscript{\text{tr}}}s-2 or C\text{\textsubscript{\text{tr}}}s-4) based on drug half-lives. Emergent HIV-1 were genotyped by deep 
sequencing and a 2% threshold.

**Results.** In these experiments, constant drug concentrations corresponding to 
full adherence (C\text{\textsubscript{\text{tr}}}s-2) did not lead to VB. Using C\text{\textsubscript{\text{tr}}}s-2 concentrations for one week fol-
lowed by constant C\text{\textsubscript{\text{tr}}}s-4 exposures for 4 weeks, DTG+3TC had VB and emergence of 
M184V/I in reverse transcriptase (RT) but there was no VB for BIC+FTC+TAF. Using 
alternating drug exposures of C\text{\textsubscript{\text{tr}}}s (weeks 1 and 3) and C\text{\textsubscript{\text{tr}}}s-2 or C\text{\textsubscript{\text{tr}}}s-4 (weeks 2, 4, 
and 5), VB was not observed with BIC+FTC+TAF and VB was decreased or delayed 
with DTG+3TC compared to DTG+3TC held at C\text{\textsubscript{\text{tr}}}s-2 or C\text{\textsubscript{\text{tr}}}s-4. Resistance develop-
ment was observed in some cultures with VB; 1 culture with BIC+FTC+TAF had 
G163R in IN and 19 cultures with DTG+3TC had INSTI and RT resistance including 
10 with M184V/I.

Table 1. Summary of Breakthrough Frequency and Resistance Development

**Conclusion.** BIC+FTC+TAF has high in vitro forgiveness and consistent protec-
tion of INSTI and RT resistance during simulating short lapses in adherence. 
Higher DTG+3TC exposure, whether constant or intermittent, was better at 
preventing or delaying VB than lower DTG+3TC exposures, but DTG+3TC was less 
forgiving than BIC+FTC+TAF. Prevention of viral replication and resistance develop-
ment is necessary to maintain lifelong viral suppression, particularly in the real world 
where drug adherence is often imperfect.

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1449. Frequency and Antimicrobial Susceptibility of Coagulase-Negative 
Staphylococcal (CoNS) Species Isolated from Clinical Specimens in United States 
and European Hospitals

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Session: P-66.Resistance Mechanisms

**Background.** CoNS represent an important cause of bloodstream infections, 
osteosarticular infections, foreign-body associated infections and endocarditis. We 
evaluated the frequency of CoNS species and the activity of dalbavancin (DALB) in 
comparison to vancomycin (VAN), daptomycin (DAP) and other agents against a large 
collection of CoNS isolates.

**Methods.** 5,088 CoNS isolates causing clinically significant infection were con-
secutively collected from 122 medical centers located in the United States (79 centers) 
and Europe (43 centers in 21 nations) over 6 years (2014-2019) and susceptibility tested 
with CLSI 2020 or FDA breakpoints. Institutions were then stratified into 
categories with CLSI breakpoint of outbreaks with emerging resistance.

**Results.** Most isolates were from bloodstream (BSI, 53.3%) or skin/skin structure 
infections (28.5%). S. epidermidis was the most common species overall (54.6%; 
Table) and for BSI (61.3%). The second most common species were S. lugdunensis 
overall (12.3%) and S. hominis for BSI (14.7%). DALB (MIC\text{\textsubscript{\text{MIC}}} \text{\textsubscript{\text{MIC}}}, 0.03/0.06 mg/L) 
inhibited > 99.9% of CoNS isolates at the susceptible (S) breakpoint established by 
CLSI for S. aureus (≤ 0.25 mg/L) and was 8-fold more active than DAP (MIC\text{\textsubscript{\text{MIC}}} > 
0.25/0.5 mg/L), ≥ 99.9% S and 32-fold more active than VAN (MIC\text{\textsubscript{\text{MIC}}} \text{\textsubscript{\text{MIC}}}, 1/2 mg/L; > 
99.9% S). Linezolid was active against 98.7% of isolates (MIC\text{\textsubscript{\text{MIC}}} 0.5/1 mg/L). All 
species were inhibited at 0.25 mg/L of DALB, except S. epidermidis (> 99.9%) 
S. warneri (98.9%, Table). The most DALB-S species were S. capitis and S. sim-
ulant (MIC, 0.03/0.03 mg/L for both species), whereas the highest DALB 
MIC\text{\textsubscript{\text{MIC}}} \text{\textsubscript{\text{MIC}}} values were observed with S. haemolyticus and S. saprophyticus (MIC\text{\textsubscript{\text{MIC}}} > 
0.06/0.12 mg/L and highest MIC of 0.25 mg/L for both species). In contrast, 47.8% of 
S. epidermidis and 34.7% S. haemolyticus exhibited decreased susceptibility to VAN 
(MIC ≥ 2 mg/L), and 23.8% of S. capitis and 28.4% of S. warneri showed decreased 
susceptibility to DAP (MIC ≥ 1 mg/L). Overall oxacillin-S rate was 39.3%, varying 
from 3.0% for S. saprophyticus to 95.4% for S. lugdunensis. In general, BSI isolates 
were slightly less S than non-BSI isolates.

**Conclusion.** Antimicrobial susceptibility varied widely among CoNS species. 
DALB exhibited potent in vitro activity against all CoNS species.

| Table 1 |

**Disclosures.** Helio S. Sader, MD, PhD, A. Menarini Industrie Farmaceutiche 
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Ifosfamide (A/R) Relebactam (I/R) Ertapenem (E/R) 

1450. Frequency of Carbapenem-resistant Pseudomonas aeruginosa Among 
Respiratory Pathogens Impacts First-Line Beta-Lactam Susceptibility: 
Potential Role for Ceftolozane/Tazobactam (C/T) and/or Imipenem/ 
Relebactam (I/R)

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Session: P-66. Resistance Mechanisms

**Background.** Carbapenem-resistant P. aeruginosa (CRPA) are associated with 
improved mortality and impose significant treatment challenges for clinicians. Among 
CRPA, co-resistance to 1 line antipseudomonal agents piperacillin/tazobactam (TZP) 
and cepofepime (FEP) is common and often results in delays to timely effective therapy. 
A simple strategy for identifying patients at risk for suboptimal therapy is evaluation 
of institutional or unit specific frequency of CRPA. The purpose of this analysis is to 
identify beta-lactam (BL) susceptibility trends based on CRPA frequency 
in diverse care units (ICU).

**Methods.** In 2016–2019, ~20 US institutions per year submitted up to 250 con-
sective, aerobic or facultatively anaerobic, gram-negative pathogens from blood, 
inguinal, and lower respiratory tract infections as part of the Study 
for Monitoring Antimicrobial Resistance Trends. A total of 871 P. aeruginosa (PA) 
isolates were collected from lower respiratory tract specimens obtained from ICU 
patients. MICs were determined using CLSI broth microdilution method and inter-
preted with CLSI 2020 or FDA breakpoints. Institutions were then stratified into 
one of three categories based on CRPA frequency: CRPA rates ≤20% (CR1), 21– 
40% (CR2), and ≥41% (CR3). BL susceptibility was then evaluated relative to CRPA 
frequency.

**Results.** Thirty-seven (46%), 25 (31%), and 18 (23%) institutions were stratified 
into CR1, CR2, and CR3, respectively. Overall, CRPA was identified in 28.4% of all 
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Disclosures. Chetan Jinadatha, MD, MPH, AHRQ (Research Grant or Support) Department of Veterans Affairs (Other Financial or Material Support, Owner: Department of Veterans Affairs). Licensed to: Xenex Disinfection System, San Antonio, TX; Inventor (Other Financial or Material Support, Methods for organizing the disinfection of one or more items contaminated with biological agents) NIH/NINR (Research Grant or Support) NSF (Research Grant or Support) Xenex Healthcare Services (Research Grant or Support).

1452. Molecular Profile of β-Lactamase Genes and Siderophore-Dependent Iron Transporter Genes of Cefiderocol High MIC Isolates from SIDERO-WT Studies
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Table 2. Antibiotic Resistance Gene Profiles of Sequence Type 2 (ST2) isolates in H1 and H2.

**Table 1.** Antimicrobial Drug Resistance Profiles of all Acinetobacter Sequence Types (STs) in H1 and H2.

**Table 2.** Antibiotic Resistance Gene Profiles of Sequence Type 2 (ST2) isolates in H1 and H2.