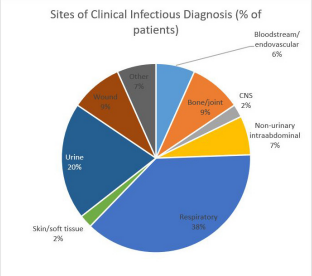

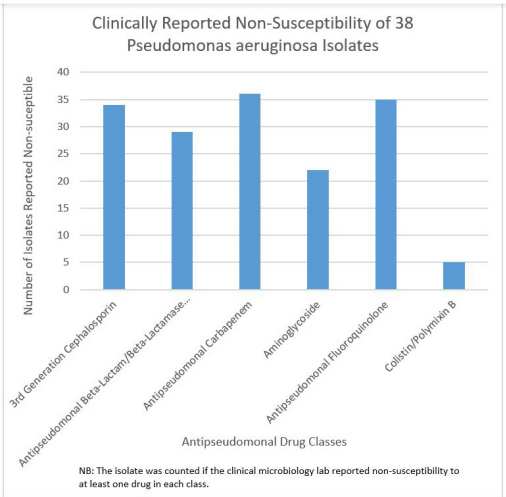

Disclosures: Samuel L. Aitken, PharmD, Melinta Therapeutoics: Grant/Research Support, Research Grant; Merck, Sharpe, and Dohme: Advisory Board; Shionogi: Advisory Board.

2249. Impact of Minimum Inhibitory Concentration on Clinical Outcomes of Daptomycin for VRE Bloodstream Infection Among Neutropenic Oncology Patients

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Background. Vancomycin-resistant Enterococcus (VRE) bloodstream infection (BSI) is a significant cause of morbidity and mortality in immunocompromised patients. This study aimed to assess the impact of daptomycin (DAP) MIC on outcomes of treatment for VRE BSI in neutropenic oncology patients.

Methods. This was a retrospective, observational, single-center, cohort study at an academic medical center. Included: age ≥ 18, neutropenia, admitted to oncology unit, and DAP for VRE BSI. Excluded: death within 24 hours after initiation of DAP, polymicrobial BSI, and linezolid use for > 48 hours before DAP initiation. Patients with VRE BSI 2008–2018 were identified using a report from the micro lab. Data were collected by electronic medical record review. The primary outcome of the study was clinical success, defined as culture sterilization, hypotension resolution, defervescence, and no need to change DAP due to persistent signs/symptoms of infection. Patients were analyzed according to DAP MIC ≤ 2 vs. ≥ 4 mg/L. Multivariable logistic regression analysis was performed to identify factors associated with clinical success.

Results. 44 patients met study criteria (MIC ≤ 2, n = 26; MIC ≥ 4, n = 18). Mean age was 58 years, 59% were male, and median ANC was 0. Median Charlson Comorbidity Index Score and Pitt Bacteremia Score (Pitt) were 5 and 1, respectively. 34% required ICU admission. More patients achieved clinical success with MIC ≤ 2 (88% vs. 56%; P = 0.03). Time to success (2.4 vs. 4 days, P = 0.02) and time to culture sterilization (2.2 vs. 2.9 days, P = 0.24) were shorter with MIC ≤ 2. Mortality was similar between groups (31% vs. 33%). Time to culture sterilization (P = 0.008), neutropenia resolution (P = 0.02), MIC group (P = 0.096), and Pitt (P = 0.52) were included in the multivariable model.

Conclusion. DAP MIC should be considered when choosing therapy for VRE BSI among neutropenic oncology patients, particularly those expected to have prolonged neutropenia and those with persistently positive cultures.

	Success (n=33)	Failure (n=11)	p
Age	58	58	0.55
ICU, %	30	45	0.47
Serum creatinine, mg/dL	0.75	1.2	0.32
Pitt	1	2	0.02
MIC ≤ 2, %	70	27	0.03
Time to sterilization, days	2.3	4.7	<0.001
Time to defervescence, days	1.55	2.13	0.87
Neutropenia resolution, %	45	0	0.01
DAP dose, mg/kg	7.3	7.6	0.74

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

2250. Combination Vancomycin Plus Cefazolin for Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections

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Background. Combination β-lactam and vancomycin (VAN) prevent the emergence of resistance and result in synergistic antimicrobial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) *in vitro*. We sought to provide clinical translation to these data and determine if patients with MRSA bloodstream infection (BSI) treated with VAN + cefazolin (VAN/CFZ) via our MRSA BSI clinical pathway had improved clinical outcomes compared VAN alone.

Methods. Multicenter, retrospective, comparative cohort study from 2006 to 2019 in adults with MRSA BSI treated with VAN for ≥ 72 hours. VAN/CFZ was defined as VAN + CFZ within ≤ 72 hours of index culture for ≥ 24 hours. Other β-lactams were allowed for < 48 h in the VAN/CFZ group. The VAN alone group could not have other β-lactams within 7 days of treatment initiation. The primary outcome was clinical failure defined as a composite of 30-d all-cause mortality, 60-day recurrence, and persistent BSI (≥ 7 days). The independent effect of VAN/CFZ on clinical failure was evaluated with multivariable logistic regression. The primary safety endpoint was nephrotoxicity within 7 days of treatment initiation.

Results. A total of 237 patients were included (104 VAN/CFZ, 133 VAN). The most common BSI sources were skin/soft tissue (29.1%), IV catheter (21.9%), osteoarticular (20.3%) and infective endocarditis (16.0%). Demographic and clinical characteristics were similar between groups except VAN/CFZ had a higher median APACHE II score (18 vs. 13, P = 0.011). VAN/CFZ patients were also more likely to have received an infectious disease consult (100% vs. 81.2%, P < 0.001). Median (IQR) duration of CFZ was 115 (87–164) hours. After controlling for age, APACHE II score, ID consult and infection source, VAN/CFZ was associated with reduced odds of clinical failure (aOR 0.425, 95% CI 0.228, 0.792). Bivariate outcomes are shown in the table:

Conclusion. Patients with MRSA BSI treated with VAN/CFZ vs. VAN experienced fewer clinical failures, supporting additional studies evaluating the role of adjuvant CFZ for MRSA BSI.

	VAN/CFZ n=104 n (%)	VAN n=133 n (%)	P value
Clinical failure	26 (25.0)	49 (36.3)	0.052
30-d mortality	8 (7.7)	11 (8.3)	0.871
60-d recurrence	7 (6.7)	16 (12.0)	0.171
BSI ≥ 7 d	17 (16.3)	32 (24.1)	0.146
Nephrotoxicity	4 (3.8)	10 (7.5)	0.234

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

2251. Estimating the Need for Novel Gram-Negative Active Antibiotics in US Hospitals

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Background. Assessing the unmet need for novel antibiotics could inform appropriate utilization, enrollment in trials and ensure balance in aligning incentives and investments in therapeutic development.

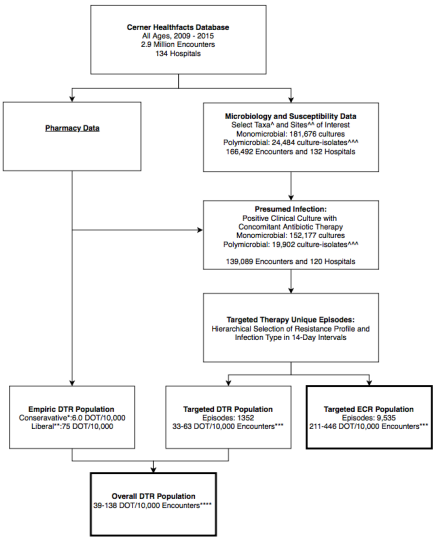
Methods. The *Cerner Healthfacts* electronic health record repository was queried to identify inpatient treatment opportunities for Gram-negative active agents (GNAA) displaying either difficult-to-treat resistance (DTR; resistance to all β-lactams including carbapenems and fluoroquinolones) or extended-spectrum cephalosporin resistance (ECR). The former was quantified by aggregating episodes of confirmed DTR infection (i.e., DTR strain isolated and concomitant antibiotic(s) received) or suspected (i.e., 1–2 days of empiric colistin/polymyxin-B or aminoglycosides and no DTR pathogen isolated). Aggregate days of therapy (DOT) were reported as a range, multiplying episodes by site-specific or uniform 14-day treatment durations, respectively. Recursive partition and cluster analyses were performed for hospital characteristics and contributions of outbreaks to DTR treatment opportunities, respectively.

Results. Between 2009 and 2015, across 2,996,271 encounters, 1,352 episodes of potential targeted treatment were identified, which combined with empiric treatment episodes, represent 39–138 DOT/10,000 encounters for a DTR-GNAA. Similarly, 9,535 episodes of potential targeted therapy for an ECR-GNAA were identified (representing 211-466 DOT/10,000 encounters). The most common candidate site and pathogens for DTR-GNAA were lower respiratory and *A. baumannii* and *P. aeruginosa*

respectively; DTR bloodstream infections displayed the highest crude mortality at 45%. *Enterobacteriaceae* urinary infections dominated the ECR group. Teaching hospitals with ≥100 beds were the most likely to encounter a DTR infection; potential outbreaks contributed to 10.6% of DTR treatment opportunities.

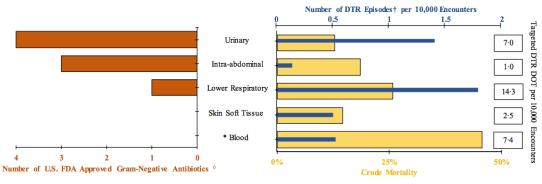
Conclusion. The candidate population for new antibacterials directed against highly resistant GN infections with limited treatment options is small but critical, indicating a role for non-revenue-based strategies to develop more effective antibiotics, as well as mechanisms to support trials that address real-world unmet needs.

Figure 1: Flowsheet demonstrating selection of empiric and targeted therapy episodes



Legend: To estimate the targeted patient population microbiology and susceptibility data were merged with pharmacy data to identify presumed infections. Using cultures that were presumed to be infection the hierarchical algorithm was applied to identify unique infection episodes based on the most resistant isolate in clinical cultures over 14-day intervals per encounter. Targeted and empiric DTR estimates were merged to determine the overall DTR population. ^*Acinetobacter baumanii* complex, *Pseudomonas aeruginosa, and Enterobactericeae*, ^^Sites of Interest: Blood, Gastrointestintal, Urine, Intra-abdominal, Skin and Soft Tissue, Respiratory, Secondary Bacteremia and Other ^^^Polymicrobial counts represent each isolate identified in a culture individually. *****Conservative estimate based on 1-2 days of colistin/polymyxin-B, ******Liberal estimates based on 1-2 of colistin/polymyxin-B and aminoglycosides (amikacin, tobramycin, and gentamicin). *******Lower bound determined with site-specific DOT multiplier and upper bound limited based on 14-day multiplier for all sites ********Overall market is the summation of conservative empiric market and targeted DTR (site specific multiplier) and upper bound limited based on summation of liberal empiric market and targeted DTR (14-day multiplier for all sites)

Figure 2: DTR Episodes and Crude Mortality Compared to the Number of U.S. FDA Approved Gram-Negative Active Antibiotics by Site Since 2014

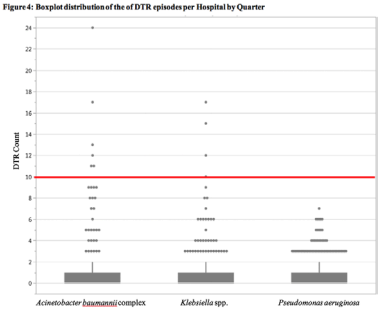


Legend: (Left) horizontal bar graph quantifying FDA approved antibiotics for gram-negative infections approved since 2014 by site. (Right) For the DTR population, mortality estimates were compared with prevalence of DTR infection by site. Thin blue bars represent DTR episodes per 10,000 encounters by site. Thick yellow bars represent associated DTR mortality. Bloodstream infections had the highest mortality rate. Despite lower respiratory tract infection being the most prevalent only one novel FDA gram-negative antibacterial has been approved for this indication. ◊ FDA approved antibiotics since 2014 by site: Complicated Urinary Tract Infections (cUTI): ceftolozane-tazobactam, ceftazidime-avibactam, meropenem-vaborbactam, plazomicin, Complicated Intra-Abdominal Infections (cIAI): ceftolozane-tazobactam, ceftazidime-avibactam, eravacycline, and Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia (HABP/VAP): ceftazidime-avibactam † Includes all infection types per site. "Other" infection site not included in this visualization. * 34 of 158 (21.5%) blood stream infections are secondary to respiratory (n=17), urinary (n=14), skin and soft tissue (n=2), and intra-abdominal (n=1) sites

Figure 3: Heat Map of DTR and ECR Episodes per 10,000 Overall Inpatient Encounters by Species and Site

Legend: The prevalence of DTR and ECR episodes were stratified by site and by species. Boxes represent species-specific days of therapy. The DTR-active antibiotic market is found to be concentrated around *Acinetobacter baumannii* and *Pseudomonas aeruginosa* lower respiratory tract infections and *Enterobacteriaceae* urinary tract infections. The carbapenem-sparing antibiotic market (represented by ECR infection) is found to be concentrated around *Enterobacteriaceae* urinary tract infections. The targeted therapy group for DTR *Stenotrophomonas maltophilia, Burkholderia* and *Achromobacter* spp was < 1 DOT/10,000 encounters each.

Figure 4: Boxplot distribution of the of DTR episodes per Hospital by Quarter



Legend: Hospitals were clustered and evaluated by quarter to identify species level outbreaks. Red line represents an arbitrary outbreak threshold defined as hospital quarters with 10 or more DTR episodes per organism. *Acinetobacter baumannii* complex was the species with the highest episodes in a single quarter (24) and 6 hospital quarters with outbreaks. *Klebsiella* species mad a max of 17 per quarter and 4 hospital quarters with an outbreak while *Pseudomonas aeruginosa* had a max of 7 per quarter and no hospital outbreaks.

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

2252. Patient Preferences for Triazole Antifungals in the Treatment of Invasive Mold Infection: A Discrete Choice Experiment

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Background. Invasive mold infections (IMIs) are an increasing cause of morbidity and mortality worldwide.[1] Pharmacological differences among the currently available mold-active triazoles make treatment selection complex.[1] To the best of our knowledge, this is the first study to assess patient preferences for mold-active triazoles in IMI treatment.

Methods. Patients were included if they were aged ≥ 18 years with investigator-confirmed invasive aspergillosis or invasive mucormycosis; had received voriconazole, isavuconazonium sulfate or posaconazole within ≤ 1 week previously; and were outpatients for ≥ 3 weeks. Participants were presented with 14 choice cards, each with two hypothetical treatments with varying levels of attributes, and asked to select their preferred treatment. Preference weights for attribute levels were analyzed using conditional logit regression and used to calculate the impact of changes in attribute levels on patient choices; relative attribute importance (RAI); and patient willingness to pay (WTP; monthly out-of-pocket cost) for an attribute improvement.

Results. Of 50 participants, 52% were female and the mean age was 47.3 years; 40%, 40%, and 28% had used posaconazole, voriconazole and isavuconazonium sulfate, respectively (Figure 1). Route of administration (27% RAI), treatment duration (22% RAI), and chance of symptom relief after treatment (20% RAI) were the most important attributes for patients (Figure 2). The odds ratios for patients choosing oral suspension or tablets/capsules over IV infusion were 5.6 and 4.5, respectively ($P < 0.001$) (Figure 3); patients were willing to pay an additional $205/month or $180/month out of pocket for these respective routes of administration over IV (Figure 4). The odds ratio for patients choosing a 30-day over a 90-day treatment were 4.1 ($P < 0.001$) (Figure 3); this decrease in duration was valued by patients at $168/month (Figure 4). For a 50% vs. 30% chance of symptom relief, the odds ratio was 3.5 ($P < 0.001$) (Figure 3) and WTP was $147.89/month (Figure 4).

Conclusion. Patients considered route of administration, treatment duration and chance of symptom relief to be the most important IMI treatment attributes among mold-active triazoles.

[1]***Jenks JD et al.*** (2019) Med Mycol 57:S168–S178

Figure 1. Patient demographics and disease characteristics

	N=50
Demographics	
Age in years, mean (SD)	47.3 (11.5)
Female, n (%)	26 (52.0)
White or Caucasian, n (%)	22 (44.0)
College/associate's or higher degree, n (%)	43 (86.0)
Full-time employment, n (%)	35 (70.0)
Commercially insured, n (%)	45 (90.0)
Disease and treatment characteristics	
Current health, n (%)	
Very good	10 (20.0)
Good	20 (40.0)
Fair	13 (26.0)
Poor	7 (14.0)
Comorbidities, n (%)	
Asthma or chronic obstructive pulmonary disease	4 (8.0)
Diabetes (type 1 or 2)	4 (8.0)
Blood cancers*	3 (6.0)
Multiple myeloma	2 (4.0)
Non-Hodgkin's lymphoma	1 (2.0)
HIV/AIDS	1 (2.0)
Born with immunodeficiency	0 (0.0)
Other†	5 (10.0)
None of the above	38 (76.0)
Current or most recent IMI treatment, n (%)	
Posaconazole	20 (40.0)
Voriconazole	20 (40.0)
Isavuconazonium sulfate	14 (28.0)
Other treatments or medical procedures ever received, n (%)	
Corticosteroids	11 (22.0)
Stem cell transplantation (including bone marrow transplantation)	2 (4.0)
Solid organ transplantation	0 (0.0)
Mechanical ventilation	0 (0.0)
Other‡	6 (12.0)
None of the above	38 (76.0)

IMI, invasive mold infection; NSAIDs: non-steroidal anti-inflammatory drugs; SD: standard deviation
*Including acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, non-Hodgkin's lymphoma, Hodgkin's lymphoma, multiple myeloma, and other blood cancers
†Other comorbidities included spondylolisthesis, spinal stenosis, herniated discs, rheumatoid arthritis, and fibromyalgia
‡Including spine surgery, NSAIDs, etanercept, dapagliflozin, methotrexate, metformin, lenalidomide, daratumumab, dexamethasone, melphalan, R-CHOP (rituximab with cyclophosphamide, doxorubicin, vincristine and prednisone), adalimumab, hydroxychloroquine, and abacavir