compared with those infected with isolates showing reduced MTZ susceptibility (60.5%; $P = 0.004$.) In multivariate logistic regression after controlling for disease severity, patients infected with strains displaying reduced MTZ susceptibility and treated with MTZ were more likely to experience treatment failure compared with patients with susceptible isolates (OR = 6.8; 95% CI:1.96–23.8; $P = 0.003$). In patients given non-MTZ-based therapies, reduced susceptibility to MTZ was not predictive of failure to other treatments.

Conclusion. This is the first report to demonstrate that increased clinical failure rates for MTZ monotherapy are associated with reduced susceptibility to MTZ.

Disclosures. **K. Garey**, Summit Therapeutics: Collaborator, Research support.

711. Molecular Epidemiology of Daptomycin Nonsusceptibility in Methicillin-Resistant *Staphylococcus aureus* (MRSA) Bacteremia

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Background. While methicillin resistance in *S. aureus* strains is prevalent, non-susceptibility to vancomycin and daptomycin, first-line treatments for bacteremia, has emerged as well. Little is known about the molecular epidemiology of daptomycin resistance in *S. aureus* strains.

Methods. A retrospective study was conducted at an 800-bed hospital in Detroit, Michigan. Blood isolates of *S. aureus* were obtained over time in patients with persistent bacteremia. Isolates were initially classified as MRSA/MSSA and MIC testing was done by the clinical microbiology laboratory; MICs were reconfirmed by a separate laboratory using Etest strips and microdilution broth testing. Non-susceptibility to daptomycin was defined as an MIC > 1 mg/mL. Isolates from each patient were also assessed for genomic similarity using pulse field gel electrophoresis (PFGE) and placed in the same PFGE group if they were [3] 80% similar by Dice coefficient. Whole genome sequencing (WGS) on isolates and template strain ATCC29213 was done by the Applied Genomics Technology Center.

Results. There were 27 isolates from seven patients in the following distribution: six isolates each from Patients 1 and 2; three isolates each from Patients 3, 4, and 5; five isolates from Patient 6; and one isolate from Patient 7. All isolates from Patients 1 and 3 ($n = 9$) were classified as MSSA strains and the remainder were MRSA strains. Daptomycin nonsusceptible strains were found in the initial isolate on therapy in two patients and the MIC increased from first to last isolates in the other five patients. A PFGE dendrogram comparing isolates within each patient and with established CDC lineages determined that (1) each patient's first and last isolate remained within the same strain type and (2) the PFGE groups were USA100 ($n = 8$), USA300 ($n = 7$), USA900 ($n = 6$), and USA1000 ($n = 3$). WGS revealed the presence of vraSR, mprF, dltA, cls2, and gdpD, genes implicated in resistance to both vancomycin and daptomycin. However, gdpD was not detected in isolates classified as MSSA.

Conclusion. No genetic modification of strains from each patient was seen between the first isolate obtained and the last. The presence of cell wall regulation genes in both daptomycin susceptible and nonsusceptible strains suggests gene upregulation.

Disclosures. **M. J. Zervos**, Merck: Consultant and Grant Investigator, Grant recipient.

712. Identification of a Novel Tedizolid Resistance Mutation in *rpoB* of Methicillin-Resistant *Staphylococcus aureus*

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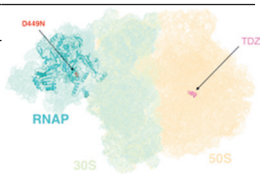
Background. Tedizolid (TDZ) is an oxazolidinone antimicrobial with broad-spectrum activity against Gram-positive bacteria including methicillin-resistant *S. aureus* (MRSA). Resistance to TDZ is uncommon but mutations in the 23S rRNA target as well as in the transferable rRNA methyltransferase gene *cfr*, which also mediate resistance to linezolid and chloramphenicol have been implicated. The objective of this study was to determine whether other TDZ resistance pathways exist in MRSA.

Methods. Using a well-characterized MRSA strain, N315, we selected for TDZ resistance by serial passage in escalating concentrations of TDZ in Mueller Hinton broth (MHB) starting with 0.5× the MIC. Once visible growth was achieved a sample of the broth was diluted 1:1,000 into fresh MHB with twice the previous concentration of TDZ until an isolate with an MIC of ≥4 mg/mL was recovered. This MIC was selected since it is 1 dilution above the breakpoint for resistance ≥2 mg/L). This isolate was subjected to whole genome sequencing (WGS) and MICs to other antimicrobials were assessed. Homology modeling was performed to evaluate the potential impact of the mutation on target protein function.

Results. After 10 days of serial passage we recovered a stable mutant with a TDZ MIC of 4 mg/L. WGS revealed a single nucleotide variant (A1345G) in the rpoB gene corresponding to an amino acid substitution at D449N. The following table and figure summarize the changes in drug susceptibility between the parent and evolved strain and reveals the location of the amino acid substitution relative to the TDZ binding site.

	MIC (mg/L)	
Drug	**N315**	**N315-TDZ4**
Chloramphenicol	**8**	**128**
Doxycycline	0.125	0.125
Linezolid	**2**	**8**
Moxifloxacin	0.0625	0.0625
Rifampin	0.001	0.001
Tedizolid	**0.25**	**4**
Vancomycin	0.5	1



Conclusion. We have identified a novel mutation in the RNA polymerase gene, rpoB, that mediates oxazolidinone and chloramphenicol resistance. This variant lies outside of the rifampin resistance determinant clusters of rpoB that span from 1,384 to 1,464 and 1,543 to 1,590, and as expected did not affect rifampin susceptibility. The underlying molecular mechanism by which this single nucleotide variant confers TDZ resistance remains unclear but may involve transcriptional modulation by altered sigma factor binding.

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

713. Vancomycin Heteroresistance in Coagulase Negative Staphylococci (CoNS) Causing Central Line-Associated Bloodstream Infection (CLABSI) in Pediatric Patients with Leukemia

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Background. Heteroresistance to vancomycin in *Staphylococcus aureus* may be associated with poor response to therapy. Although CoNS are the most important CLABSI pathogens in children with leukemia, and treatment failure is common, little is known about the frequency or clinical significance of heteroresistance. This is a retrospective study to evaluate frequency, risk factors and clinical impact of heteroresistance in CoNS CLABSI in immunocompromised children.

Methods. The study was approved by the Institutional Review Board. All patients undergoing treatment for leukemia at St. Jude Children's Research Hospital with CoNS isolated from blood between 2010 and 2016 were eligible. The first available isolate from each blood culture episode was obtained from the clinical laboratory and tested for vancomycin heteroresistance by population analysis profiling in comparison to the hVISA strain Mu3. Clinical data were collected from the medical record for up to 9 months after the episode. Episodes with ≥2 positive cultures or a single positive culture from a single lumen CVC were classified as CLABSI. Outcomes of interest included treatment failure (death or relapse of infection) or poor response to vancomycin therapy (persistence of bacteremia ≥1 day after initiation of vancomycin or treatment failure). Logistic regression was used to test associations between heteroresistance and exposures, and cumulative incidence analyses were used to test the effect on outcomes.

Results. A total of 74 CoNS isolates were obtained from 65 participants, 39 with ALL and 26 with AML; 25/74 (33.8%) of isolates showed showed heteroresistance. The strongest identified risk factor for infection with a heteroresistant organism was number of days of vancomycin in the preceding 60 days (OR = 1.05/day; $P = 0.035$). In the 40 CLABSI episodes, heteroresistant isolates had a higher cumulative incidence of poor response and of treatment failure ($P = 0.006$ and $P = 0.003$, respectively).

Conclusion. Vancomycin heteroresistance is common in CoNS causing CLABSI in children undergoing treatment for leukemia, and is associated with an increased risk of Treatment Failure. Further research should aim to validate this finding in an independent cohort and identify strategies to improve the diagnosis and treatment of these infections.

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714. Predictors of Influenza-Associated Hospitalization and Pneumonia in a Pediatric Population in Bangkok, Thailand

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