Conclusion. Mitochondrial dysfunction and SCVs may be under-recognized determinants of azole resistance in CG. If micro labs select single colonies from BGS for antifungal susceptibility testing, or in absence of prolonged incubation.

Disclosures. Cornelius J. Clancy, MD, Merck (Grant/Research Support) Minh-Hong Nguyen, MD, Merck (Grant/Research Support)

117. Trends in Four-class HIV Drug Resistance in Treatment-experienced Patients in the United States
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Session: O-24. New Developments in Infectious Diseases Diagnostics

Background. Despite the availability of potent antiretroviral therapy, only 56% of people living with HIV in the US were virally suppressed in 2018. Drug resistance can hinder suppression, especially among treatment-experienced patients, in whom the prevalence of 4-class drug resistance (4CR) is unknown.

Methods. Genotypic results of PhenoSense GT® Plus Integrate (Monogram Biosciences, South San Francisco, CA) obtained from Apr 2014 to Dec 2020 were used to assign susceptibility to nucleos(t)ide reverse transcriptase, non-nucleoside reverse transcriptase, integrase, and protease inhibitors (NRTIs, NNRTI, INIs, and PIs). Data were analyzed using summary statistics, 2 proportion Z test, one-way ANOVA and Tukey-Kramer; p < 0.05 was significant.

Results. Among 13,651 patients with 15,372 tests, median age was 43 years; most had HIV-1 subtype B infection (95.09%), followed by AG (1.32%). Among 12,303 patients with only one test, 4CR prevalence was 1.55%. Among 13,651 patients with more than one test, 4CR was seen in 3.64% of patients, and in 4.60% if cumulative resistance reports were assembled for each patient. Patients with 4CR were significantly older than those with less resistance.

The incidence of 4CR fluctuated, with a decline from 2.61% of patients tested in 2014 to 1.38% in 2017, an increase to 2.36% in 2018, and a decline to 1.56% in 2020. Among patients with more than one test, 21.01% gained resistance to a drug in a new class over an average of 19.5 months.

Most new resistance each year was to NNRTIs, followed by NRTIs, INIs, and PIs. The incidence of PI resistance declined for PIs from 13.34% of patients tested in 2014 to 11.82% in 2020, but increased for INIs from 14.56% in 2014 to 16.49% in 2020. The regimens expected to be suppressive in the greatest proportion of patients was dolutegravir + darunavir/ritonavir (94.51%).

Conclusion. The prevalence of 4CR has declined over time, but remains clinically relevant, particularly in older patients who may struggle with adherence due to complex regimens, comorbidities and polypharmacy. New drug classes may benefit this group. The concurrent increase in INI and decline in PI resistance may reflect changes in prescribing practices. Drug resistance may be underestimated unless cumulative resistance is determined.

Disclosures. Dusica Curanovic, PhD, Monogram Biosciences (Employee) Johny Lai, BS, Monogram Biosciences (Employee, Shareholder) Christos J. Petropoulos, PhD, Monogram Biosciences (Employee, Shareholder) Charles M. Walworth, MD, Monogram Biosciences (Employee, Shareholder)

118. Machine Learning Approaches to Predicting Treatment Outcomes for Carbapenem-Resistant Enterobacteriales in a Region with High Prevalence of Non-Carbapenemase Producers
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Session: O-24. New Developments in Infectious Diseases Diagnostics

Background. Carbapenem-resistant Enterobacteriales are a growing threat globally. Early detection of CRE is necessary for appropriate treatment and infection control measures. Many hospital labs can test for carbapenemase production; however, in some regions, including South Texas, the majority of CRE are non-carbapenemase producing (NCPE). This study had two interrelated aims to develop decision rules tailored to a region with high prevalence of NCPE to predict 1) antimicrobial resistance (AMR) from whole genome sequencing (WGS) data and 2) CRE treatment outcomes.

Methods. To better understand links between resistome, phenotypic AMR, and prediction of outcomes for CRE, we developed decision rules to build machine learning prediction models. We conducted WGS and antibiotic susceptibility testing (21 antibiotics) on CRE isolates from unique patients across 5 hospitals in the South Texas region between 2013 and 2020. Day 30 outcomes were based on desirability of outcome ranking (DOOR). The overall classification accuracies of the models are reported.

Results. Overall 146 CRE isolates were included, 97 were used to train each model, and 49 were used for validation. Among the F. pneumophila and E. coli CRE isolates that were available with susceptibility data, the majority (62%) were NCPE. For the clinical recovery model (DOOR), the combination of admission ICU status, piperacillin-tazobactam (PT) MIC > 16, presence of sul gene, and polymyxin-sparring regimens associated with an overall accuracy of 95% for having a worse DOOR. Majority (60%) of patients were empirically treated with piperacillin-tazobactam; notably, less than 33% isolates had PT MIC ≤ 16. Interestingly, combined effects of isolates that did not harbor carbapenemases, blaOXA-1, blaCTX-M-15, blaCMY, or ace(6')-ib-cr genes resulted in a decision rule with a 95.7% overall accuracy for susceptibility to PT (MIC < 16 μg/mL).

Conclusion. Herein, we used machine learning approaches to predict AMR and treatment-outcomes linked with WGS data in a region with predominantly NCPE infections. Machine learning can obtain a model that can make repeatable predictions, further data can improve the accuracy and guide tailored clinical decision-making.

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119. A Humanized Antibody Targeting the CotH Invasins is Protective Against Murine Mucormycosis
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Session: O-25. New Findings in Medical Mycology

Background. Despite antifungal therapy and surgical debridement, overall mortality of invasive mucormycosis is >40%. Currently the world is witnessing an explosion in mucormycosis in India among COVID-19 patients with an official count of 28,252 cases as of 06/07/2021. Thus, novel therapeutic modalities are needed. We previously reported on a mouse monoclonal antibody (C22) targeting CoH1 invasins being protective against mucormycosis. Here, we humanized C2 MAb and assessed its efficacy in vitro and in vivo.

Methods. The C2 (IgG1) paratopes of the heavy chain and light chain were grafted on the most suitable human IgG1 with back mutations in the paratopes needed to restore binding of humanized clones to CoH3 (by biover interferometry using Gator). Clones were compared to C2 in their ability to prevent Rhizopus delemar-induced injury to A549 alveolar epithelial and primary human endothelial cells and for enhancing human neutrophil killing of the fungus in vitro. C2 and the humanized clones were also compared for their ability to protect neutropic mice from mucormycosis induced by R. delemar or Mucor cirrhoides with and without antifungal therapy.

Results. Three humanized clones showed 10-fold enhanced binding affinity to CoH3 protein (~5 nM for humanized vs. ~50 nM for C2). One humanized clone (VX01) doubled the ability of neutrophils to kill R. delemar and resulted in ~50% reduction in host cell damage. A single low dose of VX01 (30 μg) given 24 h post infection resulted in comparable survival of 60-70% in mice infected intratracheally