648. Baloxavir Resistance: qPCR Detection of Antiviral Resistance Markers in Influenza A Virus

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Background. Influenza (flu) infections affect a large subset of the population every year and have significant impacts on the health of patients, especially those with weak or compromised immune systems such as the elderly, children, cancer patients, and transplant recipients. Baloxavir marboxil was approved in October 2018 as a novel antiviral therapy for treating flu. During clinical trials, mutations were identified at the I28D codon of the polymerase acidic (PA) protein that greatly increased the resistance of a flu strain to this novel drug. In this study, a qPCR was developed and validated to identify these resistance mutations allowing for guided therapeutic decisions.

Methods. Flu A sequences (6,175) of the PA gene from the NCBI Influenza Virus Database collected over the last 5 years were compiled and aligned. Primers and probes were designed to target the I28D codon of the PA gene, and specific probes for each codon yielding a resistant amino acid mutation (M2T, -M, and -F) were designed. Locked nucleic acid (LNA) bases were used to increase the specificity of the probes. A combination of clinical flu specimens, laboratory strains, and synthetic constructs of each potential resistance mutation were used to validate the precision, sensitivity, and accuracy of the assay in nasopharyngeal swabs.

Results. Precision cycle threshold (Ct) values for each detector were determined to have a standard deviation of less than 3 for inter-assay and less than 2 for intra-assay replicates. Sensitivity was determined to be 800 copies/mL in nasopharyngeal swabs. Accuracy was found to be 92.3%. A single laboratory strain from the H1N1 2009 wild-type strain was cross-reactive with both wild-type and resistant probes, but no circulating clinical H1N1 samples tested showed this response.

Conclusion. The precision, sensitivity, and accuracy of a qPCR for resistance mutations to baloxavir marboxil support this assay’s utility as an aid in the treatment of flu in at-risk patient groups. This assay allows for rapid detection (~24 hours) of resistance markers to aid clinicians in improving flu case outcomes.

Disclosures. All authors: No reported disclosures.

649. Prospective Validation of an 11-mRNA Host Immune Signature as a Novel Blood Test for Acute Septic Arthritis

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Background. Septic arthritis is an orthopedic emergency requiring immediate surgical intervention. Joint aspirations detect inflammatory cells within hours but often cannot distinguish between infections (e.g., bacterial) or other causes (e.g., gout). Cultures take days, so decisions about surgery are made with incomplete data. Aspirations carry risk of bacteria spreading and are often negative regardless of culture results. PP results (copy #/mL) independently correlated with the resistance profile of the strain.

Methods. A combination of clinical flu specimens, laboratory strains, and synthetic constructs of each potential resistance mutation were used to validate the precision, sensitivity, and accuracy of the assay in nasopharyngeal swabs. Precision cycle threshold (Ct) values for each detector were determined to have a standard deviation of less than 3 for inter-assay and less than 2 for intra-assay replicates. Sensitivity was determined to be 800 copies/mL in nasopharyngeal swabs. Accuracy was found to be 92.3%. A single laboratory strain from the H1N1 2009 wild-type strain was cross-reactive with both wild-type and resistant probes, but no circulating clinical H1N1 samples tested showed this response.

Conclusion. The precision, sensitivity, and accuracy of a qPCR for resistance mutations to baloxavir marboxil support this assay’s utility as an aid in the treatment of flu in at-risk patient groups. This assay allows for rapid detection (~24 hours) of resistance markers to aid clinicians in improving flu case outcomes.

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650. Relationship of a Multiplex Molecular Pneumonia Panel (PP) Results with Hospital Outcomes and Clinical Variables

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Background. The Pneumonia Panel (PP) (BioFire Diagnostics, Salt Lake City, UT) detects 15 potentially pathogenic bacteria semiquantitatively (copy #/mL), 8 viruses and 7 resistance genes from the lower respiratory tract in ≤1 hour in the laboratory. Since identification and susceptibility testing take ≥2 days, this rapid result time is very attractive; however, the clinical significance of the PP copy #/mL as well as a predictable group of PP positive but culture negative patients is unknown. We retrospectively studied the relationship of 270 PP results to culture results, clinical data and outcomes. Methods. Bronchoalveolar lavage fluid (N = 197) and endotracheal aspirates (N = 73) submitted to the UF Health Shands Hospital microbiology laboratory from June-September 2018 were frozen at −70°C, until tested on the PP. Patient data were extracted from the inpatient electronic medical record (Epic).

Results. Of 270 patients tested, 111 (41.1%) were PP bacteria positive/culture negative. PP results (copy #/mL) independently correlated with the resistance profile of the strain. When all PP pathogens were grouped by copy #/mL, ICU LOS (≥80%) was 10(6), and 10(7) combined compared with the PP-negative group (Table 2). Max daily temp on the day of culture in PP-positive groups 2 and 3 was significantly higher than the PP-negative group 1 (P = 0.0260, ANOVA, Table 1). Age, daily WBC, lowest paO2, Max FiO2, % on antibiotics (>28%) for all groups, and % with viruses in the PP were not significantly different across groups. When all PP pathogens were grouped by copy #/mL, ICU LOS was significantly longer for 10(7) copies/mL (P = 0.0088), as was BAL % polys (P = 0.0006). Max daily temp was almost significantly higher for PP-positive groups 10(5), 10(6), and 10(7) compared with the PP-negative group (Table 2, P = 0.0068). Conclusion. Hospital LOS was significantly longer and BAL % polys higher in the PP-positive group culture positive/PP positive group vs. PP-negative groups. ICU LOS and BAL % polys were significantly higher for the PP-positive groups vs. PP-negative regardless of culture results. PP results (copy #/mL) independently correlated with outcome and clinical measures.

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651. Multi-Center Evaluation of the BioFire® FilmArray® Blood Culture Identification 2 Panel for the Detection of Microorganisms and Resistance Markers in Positive Blood Culture Specimens

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Background. The BioFire® FilmArray® Blood Culture Identification 2 (BCID2) Panel is a diagnostic test that provides results for 26 bacterial, 7 fungal pathogens and 10 antimicrobial resistance (AMR) genes from positive blood culture (BCC) specimens in about an hour. The BCID2 Panel builds upon the existing BCID Panel with several additional assays that include Candida auris and an expanded AMR gene menu that provides methicillin-resistant Staphylococcus aureus (MRSA) results plus detection for mcr-1, carbapenem resistance, and ESBL. Here, we summarize studies conducted to establish clinical performance using an Investigational Use Only version of the BCID2 Panel.

Methods. Three studies were performed. The first involves prospective collection and testing of an expected ~1,000 residual PBCs at 7 US and 2 EU sites, which began in

Copies/mL Hospital LOS ≤70 days n=65 ICU LOS ≤70 days n=65 BAL % Polys ≤70 days n=65 Max Daily Temp ≤70 days n=65
Group 1: B positive/culture negative N=31 23.41 10.8414 44.11 98.91 64.31
Group 2: B positive/culture positive N=9 17.1310 9.1212 72.16 100.22 64.31
Group 3: B positive/culture positive BAL >90% 11.1513.1513.1510.0010.00
p-value (ANOVA, SAS) 0.0024 0.0007 0.0003 0.0001

*observations, not all patients had %Polys done or Daily Temps electronically available

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