A Prospective Pilot Evaluation of a Research Use Only (RUO) Prototype of a Highly Multiplexed Sample-To-Answer PCR System for the Detection of Pathogens from Positive Blood Culture

Background

Rapid identification of causative agents from positive blood culture (BPC) can aid early targeted therapy, as well as reduce mortality, length of stay, and costs associated with systemic infections. The BioFire FilmArray® Blood Culture Identification 2 (BCID2) Panel developed by BioFire Diagnostics, LLC, aims to maintain or enhance the performance of the BioFire Blood Culture Identification (BCID) Panel with 43 updated and novel assays. The 15 new assays on the BioFire BCID2 Panel include 6 bacterial analytes, 2 fungal analytes, and 7 antimicrobial resistance genes. Updated assays for retained analytes use current bioinformatics to expand coverage. Assay updates as well as modified algorithms confer improved sensitivity to the BioFire BCID2 Panel. The results from a prospective pilot study performed using a research-use-only (RUO) prototype of the BioFire BCID2 Panel are presented here.

Methods

De-identified BPC samples (<24 hours post-positivity) for which a clinician-ordered standard of care (SoC) test had been performed were enrolled and tested with RUO versions of the BioFire BCID2 Panel. At all participating sites BD BACTEC® PLUS Aerobic media was used for aerobic blood cultures. Two types of anaerobic blood culture media, BD BACTEC® Lytic Aerobic medium (LAM) and BD BACTEC® Plus Anaerobic medium (all other sites), were used. Aliquots of residual BPC and isolates were frozen for discrepancy resolution and AMR gene verification. Clinically ordered BioFire BCID2 Panel tests were performed according to SoC practices at each site.

The BioFire BCID Panel was used as the secondary comparator to resolve discrepant results for all updated analyte assays. Alternate PCR (comPCR) assays followed by sequencing were used as comparators to verify detections of AMR genes and to resolve discrepant results for novel analytes. The BioFire BCID2 Panel MRSA algorithm was compared to the Cephex Xpert® MRSA test for 30 select BPC samples.

Specimen Enrollment & Demographics

- Prospective evaluation between April 2018 – August 2018
- Study had IRB approval at all participating sites
- 387 specimens tested with the current RUO BioFire BCID2 Panel

Performance of BioFire BCID2 Panel Compared to SoC Culture Results for Bacteria and Yeast

- Greater coverage by updated genus-level assays improved concordance with SoC culture results
- No FP results of Proteus spp. with BioFire BCID2 Panel due to improved detection algorithms

Performance of BioFire BCID2 Panel Compared to Molecular Comparators for AMR Genes

- 100% confirmation of the subset of BioFire BCID2 Panel AMR gene detections evaluated by comPCR and sequence

Co-Detections in PBC: BioFire BCID2 Panel Compared to SoC

- BioFire BCID2 Panel and SoC have similar co-detection rates in aerobic and anaerobic PBC
- Enhanced coverage of the BioFire BCID2 Panel allowed detection of >98% of pathogens reported by SoC

Conclusions

The updated BioFire BCID2 Panel menu expands coverage to novel fungal and anaerobic pathogens, as well as additional AMR genes. Modified algorithms give the BioFire BCID2 Panel the ability to distinguish blood culture media contaminants such as Proteus spp. from actively growing pathogens in blood culture bottles and thus minimize FP results. With >99% specificity and >99% sensitivity, the BioFire BCID2 Panel is expected to provide accurate results for key pathogens associated with systemic infections, as well as important AMR genes with the same turn-around time as the BioFire BCID Panel.

All data presented were obtained with a development (RUO) version of the panel. The BioFire BCID Panel has not been evaluated by the FDA or other regulatory agencies for in Vitro Diagnostic use.