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Evaluation of the BioFire® FilmArray® Pneumonia Panel in ICU Patients with Suspected Ventilator-Associated Pneumonia

Contact Information:
Javier Y. Marcos, bioMérieux S.A.
javier.yugueros marcos@biomerieux.com

A. Iannello[a], C. Dubost[b], C. Weber[b], C. Alberti-Segui[b], C. Mousset[b], C. Ginocchio[c], M. Rogatcheva[c], O. Barraud[d], B. François[d], V. Moucadel[b], J. Yugueros-Marcos[a, b]

[a]Medical Diagnostic Discovery Department (MD³), bioMérieux S.A., Grenoble, France, [b]bioMérieux – BioFire R&D, Grenoble, France, [c]BioFire Diagnostics, LLC, Salt Lake City, UT, USA. [d]Dupuytren University Hospital, Limoges, France

Background

Ventilator associated pneumonia (VAP) is one of the most commonly encountered hospital acquired infections worldwide, and one of the major contributors to an over mortality in critically ill patients. Initial empirical antimicrobial therapy is often broad spectrum. Fast identification and quantification of microorganisms is of great importance to enable early effective targeted antimicrobial treatment. This trial compares the performance of the new BioFire® FilmArray® Pneumonia Panel (BPP), currently Investigational Use Only (IUO) with quantitative conventional culture (CC) and an independent real-time quantitative molecular-based method (MM), for the detection of microorganisms, in respiratory specimens collected from Intensive Care Unit (ICU) patients with VAP suspicion [1].

Methods

The study was a proof-of-concept, prospective, observational, non-randomized, multicenter clinical trial conducted between January and November 2013 in four different French Hospitals: University Hospital of Limoges, General Hospital of Brive, University Hospital of Tours and General Hospital of Angouleme. A total of 120 intensive care unit adult patients, who were intubated and had received mechanical ventilation for at least 48 h, were enrolled upon a clinical suspicion of VAP.

On the day of suspected VAP, a bronchoalveolar lavage (BAL) sample was collected according to a previously described technique [2]. Part of the BAL specimen was directly used for analysis with CC, while the remainders were aliquoted and frozen at -80°C for analysis with MM and BPP.

BPP results were compared to CC and MM (both considered as comparator methods), applying statistical analyses which included determination of Positive Percent Agreement (PPA), or Sensitivity, and Negative Percent Agreement (NPA), or Specificity, for each analyte. PPA was calculated as 100% x (TP / (TP + FN)). True positive (TP) indicates that both BPP and the comparator method had a positive result for a specific analyte, while false negative (FN) refers to BPP negative results considered positive by the comparator method. NPA was calculated as 100% x (TN / (TN + FP)). True negative (TN) indicates that both BPP and the comparator method had negative results, and a false positive (FP) indicates that BPP result was positive but the comparator result was negative. The exact binomial two-sided 95% confidence intervals were calculated (square bracket values in Figures 1, 2, 3).

CONVENTIONAL CULTURE | MOLECULAR METHOD | BIOFIRE PNEUMONIA PANEL

Seeding and counting on agar plates

Phenotypical methods for identification

Torch FilmArray, BioFire®

Time To Results

CC: 10 µL of raw BAL were directly seeded on agar plates. Culture is considered as positive when more than 10^4 CFU/mL are counted according to standard methods. Bacterial identifications were performed using phenotypical tools (i.e.: Vitek2®, …). Hands on time (HoT): 1.5h

MM: 500µL of BAL were incubated with 5µg lysin for 15min at 37°C before nucleic acid extraction. DNA was extracted from all lysates using the NucliSENS® easyMag, according to the specific B2.0.1 protocol, with an elution volume of 55µL. Real-time PCR were run by batches for each pathogen independently. HoT: 1.5h [1]

BPP: A flocked swab is dipped into the BAL specimen. It's then added into the Sample Injection Vial to load the BPP pouch. HoT: 5min

Results

A total of 117 different BAL specimens were processed by the three methods. Positive CC was obtained for 65.8% of BAL, while positive detections were observed in 79.4% with BPP and 75.4% with the independent MM. Fourteen different species were detected by the three methods, being the main isolated bacteria *S. aureus, P. aeruginosa* and *H. influenzae*. Figure 1 shows comparison of results obtained with BPP and CC , for each detected microorganism. Discrepant results (FP in yellow and FN in red) were investigated and categorized in five different groups, as shown in Figure 2. Table 1 assess concordance between BPP and CC in terms of PPA and NPA values for each analyte, considering discrepant cases within categories A, B, C and D as concordant.

Same analysis rationale was applied to compare BPP to MM (Figure 3). Discordant results were in this case categorized in 3 groups: category A (threshold discrepancy between methods), category D (BPP retested) and E (unexplained) (Figure 4). Table 2 shows PPA and NPA values for each analyte after considering categories A and D as concordant results.

Figure 1: Concordance BPP *vs.* CC

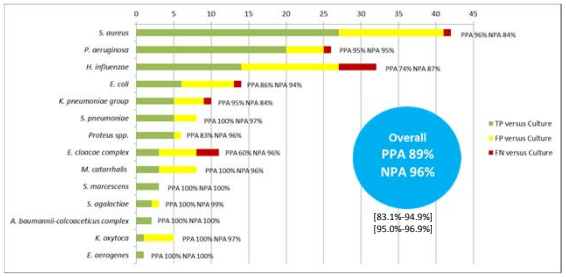
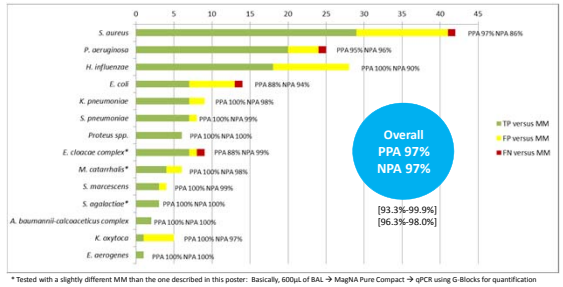


Figure 3: Concordance BPP *vs.* MM



* Tested with a slightly different MM than the one described in this poster: Basically, 600µL of BAL → MagNA Pure Compact → qPCR using G-Blocks for quantification

Figure 2: Discrepancy categories & rates overall (BPP *vs.* CC)

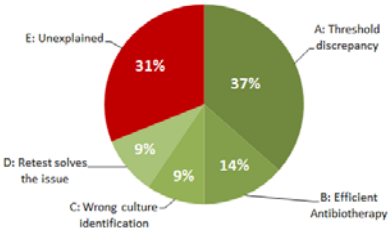


Figure 4: Discrepancy categories & rates overall (BPP *vs.* MM)

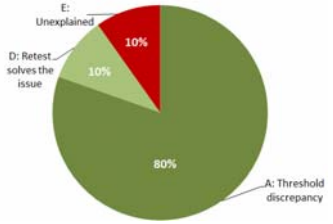
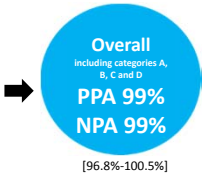


Table 1: BPP *vs.* CC concordance after discrepancy investigations

N=	117			
Target	TP culture	FN culture	TN culture	FP culture
S. aureus	35	0	75	7
H. influenzae	28	2	85	2
P. aeruginosa	24	0	91	2
E. coli	12	0	103	2
E. cloacae complex	10	0	106	1
K. pneumoniae group	10	0	107	0
S. pneumoniae	7	0	109	1
M. catarrhalis	4	0	109	4
Proteus spp.	5	0	111	1
K. oxytoca	4	0	112	1
S. marcescens	3	0	114	0
S. agalactiae	3	0	114	0
A. baumannii-calcoaceticus complex	2	0	115	0
E. aerogenes	1	0	116	0
Overall	148	2	1467	21



[96.8%-100.5%]
[98.0%-99.2%]

Table 2: BPP *vs.* MM concordance after discrepancy investigations

[100%-100%]
[99.5%-100%]

N=	117			
Target	TP MM	FN MM	TN MM	FP MM
S. aureus	30	0	85	2
P. aeruginosa	21	0	95	0
H. influenzae	18	0	98	0
E. coli	8	0	109	0
K. pneumoniae	8	0	109	0
Proteus spp.	6	0	111	0
S. pneumoniae	7	0	110	0
E. cloacae complex*	8	0	108	1
M. catarrhalis*	4	0	112	1
S. marcescens	3	0	114	0
A. baumannii-calcoaceticus complex	2	0	115	0
E. aerogenes	1	0	115	0
K. oxytoca	1	0	116	0
S. agalactiae*	3	0	114	0
Overall	120	0	1511	4

Conclusion

Results observed in this study show a very good concordance between BioFire® FilmArray® Pneumonia Panel method and Conventional Culture method. Moreover BPP shows a very high correlation with an independent real-time quantitative Molecular-based Method. With a turnaround time of only 65 minutes the new BioFire® Pneumonia® Panel can provide reliable microbiological evidence in BAL specimens. This can lead to a more appropriate management of VAP in the ICU. Information presented in this poster comes from an Investigational Use Only assay.

References/Citations

1. Molecular quantification of bacteria from respiratory samples in patients with suspected VAP. Clavel M, Barraud O, Moucadel V Clin Microbiol Infect. 2016 Sep;22(9):812.e1-812.e7. doi: 10.1016/j.cmi.2016.06.013
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3. Sanford Guide to Antimicrobial therapy , 2018