Co-Detections of Coronaviruses (CoV) with other Viruses and Bacteria in Clinical Specimens using the BioFire® FilmArray® System

TECHNICAL ::: NOTE

Introduction

Several single-analyte assays for the detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) have become available in response to the December 2019 outbreak and now world-wide pandemic of Coronavirus Disease 2019 (COVID-19) illness. In developing diagnostic algorithms, healthcare providers have been testing patients with the single analyte SARS-CoV-2 test alongside syndrome-based BioFire® FilmArray® Respiratory Panels. The purpose of this technical note is to provide information on SARS-CoV-2 detections from literature currently available (March 2020) as well as an additional analysis of clinical data with respect to observations of coronavirus co-detections with other bacteria and viruses in clinical specimens.

Literature Review

As of March 2020, there are several early reports of patients who have been diagnosed with COVID-19 illness, received a positive SARS-CoV-2 molecular test result, and were also positive for additional common respiratory pathogens. There are both comprehensive reviews and specific case reports that have documented individuals with co-detections of SARS-CoV-2 with influenza A[1], human metapneumovirus[2], *Mycoplasma pneumoniae*[3],other coronaviruses, human rhinovirus/enterovirus[4] as well as influenza B, *Legionella pneumophila*, and respiratory syncytial virus (RSV)[5].

Pathogen Co-Detections in BioFire Studies of Respiratory Panels

BioFire Diagnostics currently offers multiple BioFire Panels with the capability to detect various coronaviruses (CoV; Table 1).

Table 1. BioFire Panels Coronavirus Detections

Panel	Result Reported	Interpretation
Respiratory Panel (RP)	· Coronavirus 229E Detected · Coronavirus HKU1 Detected · Coronavirus NL63 Detected · Coronavirus OC43 Detected	· CoV-229E detected in the specimen · CoV-HKU1 detected in the specimen · CoV-NL63 detected in the specimen · CoV-OC43 detected in the specimen

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Respiratory Panel EZ (RP-EZ)	· Coronavirus Detected	· CoV-229E, CoV-HKU1, CoV-NL63, and/or CoV-OC43 detected in the specimen
Respiratory Panel 2 (RP2)	· Coronavirus 229E Detected · Coronavirus HKU1 Detected · Coronavirus NL63 Detected · Coronavirus OC43 Detected	· CoV-229E detected in the specimen · CoV-HKU1 detected in the specimen · CoV-NL63 detected in the specimen · CoV-OC43 detected in the specimen
Respiratory Panel 2 *plus* (RP2*plus*)	· Coronavirus 229E Detected · Coronavirus HKU1 Detected · Coronavirus NL63 Detected · Coronavirus OC43 Detected · Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Detected	· CoV-229E detected in the specimen · CoV-HKU1 detected in the specimen · CoV-NL63 detected in the specimen · CoV-OC43 detected in the specimen · MERS-CoV detected in the specimen
Pneumonia Panel	· Coronavirus Detected	· CoV-229E, CoV-HKU1, CoV-NL63, and/or CoV-OC43 detected in the specimen
Pneumonia Panel *plus*	· Coronavirus Detected · Middle East Respiratory Syndrome Coronavirus (MERS-CoV) Detected	· CoV-229E, CoV-HKU1, CoV-NL63, and/or CoV-OC43 detected in the specimen · MERS-CoV detected in the specimen

BioFire Diagnostics conducted prospective clinical evaluations for each of these panels to support regulatory clearance. The data from these studies is published in each panel's respective IFU. The analysis below is a closer examination of that data.

Data from the prospective clinical evaluations of various BioFire® Panels indicate that the incidence of a viral detection in a polymicrobial specimen is between 5.1% and 20.9%. The additional analyte(s) detected in these polymicrobial specimens may include a secondary virus and/or bacteria (Table 2). It should be noted that the various respiratory panels (RP, RP EZ, RP2, and RP2*plus*) contain fewer bacterial targets (3-4 targets) than the FilmArray Pneumonia Panel (18 targets), which may help to explain the lower incidence of co-detections with bacterial analytes in the RP, RP EZ, RP2 and RP2*plus* respiratory panels.

Table 2. Incidence of Additional Analyte(s) Detected in Viral Specimens from Prospective Clinical Evaluations

Panel	# of Specimens Tested	Number (%) of Specimens with:	
		Two or More Viral Detections	Mixed Viral and Bacterial Detections
RP	1117	66 (5.9%)	2 (0.2%)
RP-EZ	1049	52 (5.0%)	1 (0.1%)
RP2 / RP2*plus*	1612	192 (11.9%)	13 (0.8%)
Pneumonia / Pneumonia *plus* - *BAL*	846	12 (1.4%)	50 (5.9%)
Pneumonia / Pneumonia *plus* - *sputum*	836	25 (3.0%)	172 (20.6%)

More specifically, the incidence of a CoV (non-SARS-CoV-2) in a polymicrobial specimen is between 1.3% and 4.5%. The additional analyte(s) detected in these polymicrobial specimens may also include a secondary CoV, non-CoV viruses, and/or bacteria (Table 3).

Table 3. Incidence of Additional Analyte(s) Detected in CoV Specimens from Prospective Clinical Evaluations

Panel	# of Specimens Tested	Number (%) of Specimens with:			
		Mono-microbial CoV Detection	Multiple CoV Detections	CoV with non-CoV Viral Detection(s)	CoV with Bacterial Detection(s)
RP	1117	49 (4.4%)	1 (0.1%)	27 (2.4%)	0 (0%)
RP-EZ	1049	47 (4.5%)	0 (0%)[a]	14 (1.3%)	0 (0%)
RP2 / RP2*plus*	1612	60 (3.7%)	3 (0.2%)	72 (4.5%)	1 (0.1%)
Pneumonia / Pneumonia *plus* - *BAL*	846	15 (1.8%)	0 (0%)[b]	5 (0.6%)	8 (0.9%)
Pneumonia / Pneumonia *plus* - *sputum*	836	9 (1.1%)	0 (0%)[b]	7 (0.8%)	22 (2.6%)

[a] The BioFire® RP-EZ Panel cannot distinguish between coronaviruses, therefore the results of the comparator method (which did distinguish coronaviruses) were used to determine the type(s) of CoV detected
[b] The BioFire® Pneumonia Panel and Pneumonia Panel *plus* cannot distinguish between coronaviruses (other than MERS-CoV), therefore the results of the comparator method (which did distinguish coronaviruses) were used to determine the type(s) of CoV detected

Considerations for SARS-CoV-2

Several publications and BioFire data from previous clinical evaluations of respiratory pathogens indicates that viruses, including coronaviruses and specifically SARS-CoV-2, may be found in co-infections. Results for any diagnostic test should be used in conjunction with other clinical and epidemiological information and should not be used as the sole basis for diagnosis, treatment, or other management decisions.

Literature Cited

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4. Wang, M. *et al. Clinical diagnosis of 8274 samples with 2019-novel coronavirus in Wuhan*. http://medrxiv.org/lookup/doi/10.1101/2020.02.12.20022327 (2020) doi:10.1101/2020.02.12.20022327.

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