Introduction

Lower respiratory tract infections can be caused by an array of bacterial, viral, or fungal organisms. These infections can carry high morbidity and mortality in hospitalized patients. Rapid and accurate identification of these organisms is central to selection of the appropriate antimicrobial regimen and patient management; however, culture methods are slow and may be insensitive, and molecular tests are not available or are not routinely ordered on these specimens. We evaluated an Investigational Use Only (IUO) version of the FilmArray® Lower Respiratory Tract Infection (LRTI) Panel (BioFire, Salt Lake City, UT) for potential impact on modifications to antimicrobial therapy for respiratory pathogens in sputum and bronchioalveolar lavage (BAL) specimens.

Methods

- Respiratory specimens (57 BAL, 48 sputum) from unique patients were collected from inpatients aged 18 years and older with symptoms of a respiratory tract infection at 8 hospitals in the US.
- All specimens were tested using the FilmArray LRTI Panel, which simultaneously identifies: – 18 bacterial agents (14 reported semi-quantitatively when the target genome is present ≥10⁷ copies/mL) – 2 fungal agents (reported qualitatively) – 9 viral agents (reported qualitatively) – Select resistance mechanisms.
- Results for the FilmArray LRTI Panel were compared to standard of care (SOC) methods including bacterial culture and PCR based on standard laboratory protocol and clinician order.
- Chart review was conducted to determine type and duration of antimicrobial therapy for each patient.
- The prescribed antimicrobial therapy was compared to what antimicrobials would have been appropriate for pathogen-directed therapy, based on the FilmArray LRTI Panel result:
  - Potential modifications to antimicrobial therapy were analyzed (Table 1).
  - Hours of antimicrobial therapy avoided was documented.
  - Time from FA LRTI Panel result (or start of antimicrobial therapy, if this occurred after) to time of antimicrobial optimization based on SOC result.

Results

- Among the 105 collected clinical specimens, 96 contained sufficient clinical data to meet inclusion criteria.

Table 1. Potential Antimicrobial Modifications Based on FA LRTI Panel Results

<table>
<thead>
<tr>
<th>Potential Intervention</th>
<th>Description</th>
</tr>
</thead>
</table>
| Appropriate antimicrobial escalation | Clinically significant organism(s) or resistance mechanisms were identified on FA and were not identified via SOC.  
  - Use of FA would result in appropriate initiation of one or more antimicrobial agents.  
  - Use of FA would result in appropriate broadening of spectrum of antimicrobial therapy. |
| Appropriate antimicrobial de-escalation | Clinically significant organism(s) or resistance mechanisms were identified on FA and were not identified via SOC.  
  - FA would result in appropriate discontinuation of one or more antimicrobial agents.  
  - FA would result in appropriate de-escalation of one or more antimicrobial agents. |
| Inappropriate antimicrobial escalation/ continuation | Clinically insignificant organism(s) or resistance mechanisms were identified on FA and were not identified via SOC.  
  - FA would result in inappropriate initiation or continuation of one or more antimicrobial agents.  
  - FA would result in inappropriate broadening of spectrum of antimicrobial therapy. |
| Inappropriate antimicrobial de-escalation | Clinically significant organism(s) were identified via SOC and were not identified on FA.  
  - FA would result in inappropriate discontinuation of one or more antimicrobial agent.  
  - FA would result in inappropriate de-escalation of one or more antimicrobial agents. |
| No potential change in therapy | Concordant FA and SOC results or clinically insignificant organism(s) identified on FA.  
  - No escalation or de-escalation possible based on FA results. |

Table 2. Patients with Potential Inappropriate Antimicrobial Escalation/Continuation

<table>
<thead>
<tr>
<th>Pt.</th>
<th>SOC</th>
<th>FA</th>
<th>Potential Inappropriate Antimicrobial Escalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&gt;10,000 cfu/mL Pseudomonas aeruginosa Yeast (not Cryptococcus spp.)</td>
<td>10⁷ Pseudomonas aeruginosa mecA</td>
<td>Patient was on pip/taz. Potential for inappropriate initiation of anti-MRSA agent.</td>
</tr>
<tr>
<td>2</td>
<td>NOF</td>
<td>10⁷ E. coli Rhinovirus</td>
<td>Patient was on ertapenem. Potential for inappropriate continuation of ertapenem.</td>
</tr>
<tr>
<td>3</td>
<td>3+ Proteus NOF</td>
<td>&gt;10⁷ Proteus spp. &gt;10⁷ Staphylococcus aureus</td>
<td>Patient was not started on antimicrobials. Potential for inappropriate initiation of Gram-negative and anti-staphylococcal agent.</td>
</tr>
<tr>
<td>4</td>
<td>No growth</td>
<td>&gt;10⁷ Staphylococcus pneumoniae Pneumocystis jirovecii</td>
<td>Patient was immunocompetent and not started on antimicrobials. Potential for inappropriate initiation of anti-streptococcal agent.</td>
</tr>
<tr>
<td>5</td>
<td>Many Pseudomonas aeruginosa NOF</td>
<td>&gt;10⁷ Haemophilus Influenzae &gt;10⁷ Pseudomonas aeruginosa</td>
<td>Patient was not started on antimicrobials. Potential for inappropriate initiation of Gram-negative agent.</td>
</tr>
<tr>
<td>6</td>
<td>Many Pseudomonas aeruginosa NOF</td>
<td>&gt;10⁷ Pseudomonas aeruginosa</td>
<td>Patient was not started on antimicrobials. Potential for inappropriate initiation of Gram-negative agent.</td>
</tr>
<tr>
<td>7</td>
<td>NOF</td>
<td>&gt;10⁷ Acinetobacter baumannii &gt;10⁷ Proteus &gt;10⁷ Staphylococcus aureus mecA</td>
<td>Patient was started on ceftriaxone and vancomycin. Potential inappropriate escalation from ceftriaxone to anti-acinetobacter agent.</td>
</tr>
</tbody>
</table>

Conclusions

- Use of the FilmArray LRTI Panel in patients with a lower respiratory tract infection had the potential to lead to antimicrobial escalation in 50% of patients.
- The most common type of potential intervention was antimicrobial de-escalation, which may result in significant reductions in unnecessary antimicrobial therapy in these cases.
- As compared to SOC methods, use of the FilmArray LRTI Panel may lead to increased rates of antimicrobial therapy optimization with low risk for inappropriate therapy changes.