INTRODUCTION

• The Unyvero system is a rapid molecular diagnostics platform recently cleared by the FDA for use with Endotracheal Aspirates (EA).

• In patients where it is clinically apparent that there is a lower respiratory tract infection (LRTI) but where microbiological diagnosis has been unable to be determined a bronchoalveolar lavage (BAL) is frequently performed to obtain a deep specimen from the affected area of the lung.

• The ability to use a highly multiplexed molecular assay to quickly determine what potential pathogens are present in a BAL would be a great clinical value in urgent and difficult to treat cases of LRTI.

METHODOLOGY

• For this study Curetis, the manufacturer of the Unyvero platform, supplied an investigational use LRTI panel and installed modified software on the platform to enable analysis of BAL samples.

• The panel included Pneumocystis jirovecii but was otherwise identical to the current FDA approved LRTI panel.

• A total of 68 BAL samples were analyzed and results from the Unyvero were directly compared to standard cultures performed in the Beaumont Clinical Microbiology Laboratory.

• To calculate specificity and sensitivity all positives were considered true positives and calculations were performed for both culture and Unyvero based on that assumption.

• In this case sensitivity is a true positive rate and specificity is a true negative rate.

• A Matthews correlation coefficient (MCC) was calculated for both Unyvero and culture.

RESULTS

Table 1: Sensitivity and specificity for Unyvero results compared to culture

<table>
<thead>
<tr>
<th>Organism</th>
<th>Culture (57 samples)</th>
<th>Unyvero (52 samples)</th>
<th>Unyvero results</th>
<th>Concordent</th>
<th>Discordant</th>
<th>Positive</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>P. aeruginosa</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
<td>0%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
<td>0%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
<td>0%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>E. coli</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
<td>0%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>E. cloacae</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
<td>0%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>S. pneumoniae, K. oxytoca, E. cloacae</td>
<td>95%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
<td>0%</td>
<td>95%</td>
<td>95%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Figure 1: Concordance and discordance between Unyvero and culture

Figure 2: Unyvero time-to-result compared to culture time-to-result

Figure 3: Pathogen detection – Unyvero results compared to culture results

Figure 4: Pathogens missed by Unyvero or culture

Figure 5: Comparison between Unyvero, culture, and Gram Stain results

Table 2: Multi-organism detections by culture and Unyvero

<table>
<thead>
<tr>
<th>Organism(s)</th>
<th>Culture detected</th>
<th>Unyvero detected</th>
<th>Concordent</th>
<th>Discordant</th>
</tr>
</thead>
<tbody>
<tr>
<td>P. jirovecii, S. aureus, S. pneumoniae</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

RESULTS

• The 68 samples yielded the following results: 27 were negative by both culture and Unyvero, 26 samples were positive and concordant between culture and Unyvero, in 12 samples Unyvero detected all organisms found by culture and a total of 23 additional organisms not found via culture, in 3 samples 1 organism was found by culture but not by Unyvero (Figures 1, 3, 4).

• The overall sensitivity of Unyvero based on all positives was 95% and the specificity was 99.77% (Table 1). The MCC is 0.976.

• The overall sensitivity of culture based on all positives was 65% and the specificity was 98.25% (Table 1). The MCC is 0.797.

• The average time for standard microbiological identification of the organism in positive cultures was 2.9 days whereas the Unyvero results were available in ~5 hours (Figure 2).

CONCLUSIONS

• This study indicates that the Unyvero system, while not completely concordant with culture results from BALs, has better sensitivity and specificity than culture and can detect possible pathogens in BALs which are missed by culture.

• In addition, the time from arrival in the laboratory to actionable results is reduced by more than 2 days.

• Only one organism had a better sensitivity in culture, Moraxella, and this is likely due to the small numbers of each individual organism in this study.

• When approved by the FDA for use with BALs, this system has significant potential to reduce time till appropriate diagnosis of LRTIs. Clinical impact will be determined through routine use.

Acknowledgements

We would like to thank Curetis for providing the Unyvero reagents for this study. We would like to thank the Beaumont Clinical Microbiology Laboratory for supplying clinical specimens for this study.