ABSTRACT

Background: A multicenter study was performed to evaluate the accuracy of meropenem/vaborbactam on a MicroScan Dried Gram Negative (MGS) panel and MicroScan prompt inoculation (Prompt) methods of inoculation in the efficiency phase. For challenge, 95 Enterobacteriaceae clinical isolates were tested on MGS panels at one site. For reproducibility, a subset of 14 organisms was tested on MGS panels at each site. MGS panels were incubated at 3 ± 2°C and 29 ± 1°C in the WalkAway autoSCAN 4 instrument (WalkAway), the MicroScan autoSCAN 4–instrument (autoSCAN-4), and read visually. Frozen reference panels were read at 16–20 hours. CLSI/FDA breakpoints (µg/mL) used for interpretation of MIC results were: Enterobacteriaceae ≤ 4 µg/mL, S. aureus ≤ 0.06 µg/mL, and E. faecalis ≤ 0.06 µg/mL.

Methods: Results: When compared to frozen reference panel results, essential and categorical agreements for isolates tested in the Efficacy and Challenge phases are as follows:

<table>
<thead>
<tr>
<th>Method</th>
<th>Overall No. (%) Agreement</th>
<th>Categorical Agreement</th>
<th>MicroScan AutoSCAN 4</th>
<th>MicroScan WalkAway</th>
<th>Visual</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>E. coli</td>
<td>99.0</td>
<td>97.9</td>
<td>98.2</td>
<td>97.5</td>
<td>97.5</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>97.5</td>
<td>97.3</td>
<td>98.2</td>
<td>97.5</td>
<td>97.6</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>98.2</td>
<td>99.2</td>
<td>98.2</td>
<td>98.2</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Challenge</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>E. coli</td>
<td>99.1</td>
<td>99.2</td>
<td>99.1</td>
<td>99.2</td>
<td>99.2</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>99.1</td>
<td>99.1</td>
<td>99.1</td>
<td>99.1</td>
<td>99.1</td>
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INTRODUCTION

A multicenter study was performed to evaluate the performance of a MicroScan Dried Gram Negative (MGS) panel with meropenem/vaborbactam using Enterobacteriaceae isolates with CLSI/FDA interpretive criteria.

RESULTS

Panels

Frozen reference and MicroScan Dried Gram Neg ativ e MIC panels contained 95% of meropenem/vaborbactam 0.03/0.6–64/8 µg/mL in catalyzed Mueller-Hinton broth. Reference MICs were prepared and frozen following CLSI/ISO recommendations.

Quality Control

Quality control (QC) testing was performed daily using ATCC 25922 E. coli, ATCC 27853 P. aeruginosa, ATCC 35218 E. coli, ATCC 700603 K. pneumoniae, and E. coli BAA 1225 E. coli using subcultured clinical isolates MSL10-MD92 QC ranges based on the panel dilutions.

Panel Inoculation, Incubation, and Reading

All isolates were inoculated onto tryptic soy agar (TSA) with 5% sheep blood and incubated for 18–24 hours at 34–37°C prior to testing. Isolates were subcultured twice before testing. Incubation suspensions for each strain were prepared with the direct standardization (turbidity standard) method for MicroScan MIC and frozen reference panels. MicroScan MIC panels were also inoculated with the Prompt inoculation method.

Following inoculation, MicroScan MIC panels were incubated at 3 ± 2°C in the WalkAway system for 18 ± 2 hours. All panels were read by the WalkAway autoSCAN 4, and visually.

Reproducibility

Reproducible organisms with known results on-scale for meropenem/vaborbactam were tested in triplicate for each inoculation method on the MicroScan Dried Gram Neg ativ e panels and singly on the frozen reference panel on three different days at each site. MicroScan Dried Gram Neg ativ e MIC panels were tested using both the Prompt and Prompt inoculation methods and read on the WalkAway system, autoSCAN 4 instrument manually.

Data Analysis

Efficacy Agreement (EA) = MSDGN panel MIC within ± 1 dilution of the frozen reference MIC result. Categorical Agreement (CA) = MSDGN panel and reference categorical results (S, I, R) agree using CLSI/FDA breakpoints for Enterobacteriaceae (Table 1).

Table 1. Meropenem/Vaborbactam (CLSI M100–ED29) Interpretive Breakpoints (µg/mL)

<table>
<thead>
<tr>
<th>Organism Group</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
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<tr>
<td>Enterobacteriaceae</td>
<td>≤ 4 µg/mL</td>
<td>8–16 µg/mL</td>
<td>32 ± 16 µg/mL</td>
</tr>
</tbody>
</table>

Major Errors = Frozen MIC is S and MSDGN panel MIC is R; calculated for susceptible strains only.

Major Errors (%) = Total No. S isolates tested

No. (%) Agreement = Total No. S isolates tested

Prompt (Table 3)

For Challenge: Minimum inhibitory concentrations (MICs) were determined using the Prompt method as reference method and Prompt method as comparative methods.

Efficacy & Challenge Combined (Tables 2 and 3)

A total of 560 Enterobacteriaceae clinical isolates were tested among 3 sites using AutoSCAN and MSL10 during efficacy. For Challenge, 95 Enterobacteriaceae isolates were tested at one site. The tables below show the in vitro efficacy and challenge combined with the indicated inoculation method. A total of 560 Enterobacteriaceae clinical isolates were tested among 3 sites using AutoSCAN and MSL10 during efficacy. For Challenge, 95 Enterobacteriaceae isolates were tested at one site. The tables below show the in vitro efficacy and challenge combined with the indicated inoculation method. (See https://www.fda.gov/STIC for indicated species).

Turbidity

Categorical Agreement for Enterobacteriaceae between MSDGN panel and frozen reference panel was 97.5% (641/655 for manual method, 98.2% (643/655) for WalkAway System, 97.9% (641/655 for autoSCAN 4 instrument using the turbidity inoculation method. Categorical Agreement for Enterobacteriaceae between MSDGN panel and frozen reference panel was 98.5% (655/655) for manual method, 96.0% (649/655) for WalkAway System, 98.5% (655/655) for autoSCAN 4 instrument using the turbidity inoculation method.

Table 2. Clinical Isolates—Turbidity Inoculation Method

Read Method | Inoculation Method | No. (%) Agreement | Categorical Agreement | MicroScan AutoSCAN 4 | MicroScan WalkAway | Visual |
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</tr>
</thead>
<tbody>
<tr>
<td>WalkAway</td>
<td>Prompt</td>
<td>99.1</td>
<td>99.1</td>
<td>99.1</td>
<td>99.1</td>
<td>99.1</td>
</tr>
</tbody>
</table>

 QUALITY CONTROL

Quality Control (Table 5) Overall QC results for the MSDGN panel were 94.9–100% in range for organisms tested (Table 5). Overall QC results for frozen reference panel were 95.2–100% in range for organism tested. Table 5. Quality Control

Conclusions

This multicenter study showed that meropenem/vaborbactam MIC results for Enterobacteriaceae obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels using CLSI/FDA interpretive criteria.

This study was supported by Melinta Therapeutics Inc.