Verification of a Lyophilized Custom Sensititre Broth Microdilution Panel for Resistant Gram-negative Organisms

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INTRODUCTION

Increasing resistance in gram-negative organisms has limited available treatment options. We created a custom broth microdilution (BMD) panel for resistant gram-negative organisms (R-GN) with ThermoFisher and verified a lyophilized version of the panel against its frozen (gold standard) counterpart.

METHODS

The R-GN panel permit CLSI and EUCAST breakpoints for Enterobacteriales, Pseudomonas aeruginosa, Acinetobacter, Aeromonas, Non-Fermenters, Burkholderia cepacia, and Stenotrophomonas maltophilia. Ceftazidime/avibactam, cefotazone/tazobactam, colistin, imipenen/relebactam, meropenem/vaborbactam, plazomicin and tigecycline were included. R-GN (44 Enterobacteriales, 20 Pseudomonas aeruginosa, 19 Acinetobacter, 7 Aeromonas, 10 Non-Fermenters, 6 Burkholderia cepacia, and 9 Stenotrophomonas maltophilia) were tested on the lyophilized panel to determine very major errors (VME), major errors (ME), minor errors (MinE), and categorical/essential agreements (CA/EA) compared to frozen BMD. Acceptability was determined using Cumitech31A thresholds (≤90% EA/≤90% CA/≤7% MinE+ME) and calculating 95%CI using CLSI/EUCAST breakpoints.

RESULTS

The lyophilized panel performed well with some exceptions. A summary of EA/CA/VME/ME/MinE results for newer agents within range (green), within range taking 95%CI into account (orange) and out of range (red) is shown (Table 1). For Enterobacteriales, Pseudomonas aeruginosa, Acinetobacter, Aeromonas, and non-fermenters: ceftazidime/avibactam, imipenen/relebactam, meropenem/vaborbactam, and plazomicin all had acceptable EA/CA/VME/ME/MinE for all species; cefotazone/tazobactam has acceptable EA/CA/VME/ME/MinE except for Pseudomonas aeruginosa/Acinetobacter, colistin has acceptable EA/CA/VME/ME/MinE except Pseudomonas aeruginosa; meropenem/vaborbactam had acceptable EA/CA/VME/ME/MinE except for non-fermenters; tigecycline had acceptable EA/CA/VME/ME/MinE except for Enterobacteriales, Acinetobacter, and Aeromonas. For Burkholderia cepacia and Stenotrophomonas maltophilia, imipenen/relebactam, meropenem/vaborbactam, and tigecycline had acceptable EA/CA/VME/ME/MinE but ceftazidime/avibactam, cefotazone/tazobactam, colistin, and plazomicin had at least one parameter outside of its threshold.

CONCLUSIONS

Although the lyophilized panel generally performed well, it does not replace the gold standard frozen BMD for all drug-organism combinations.

Table 1. Table showing results of the lyophilized panel compared to the frozen panel. A green cell indicates point estimate agreement within the threshold, yellow cell indicates point estimate disagreement with the threshold but agreement within the confidence interval, and red cells indicate disagreement with the threshold including confidence intervals. Grey cells show where there was not enough specimen for that category (i.e. grey VME means no resistant bacteria).

DISCUSSION AND CONCLUSIONS

The lyophilized panel performed well with some exceptions:
- For Enterobacteriales, Pseudomonas aeruginosa, Acinetobacter, Aeromonas, and non-fermenters
- Ceftazidime/avibactam, imipenen/relebactam, and plazomicin had acceptable EA/CA/VME/ME/MinE for all species
- Cefotazone/tazobactam has acceptable EA/CA/VME/ME/MinE except for Pseudomonas aeruginosa/Acinetobacter
- Colistin has acceptable EA/CA/VME/ME/MinE except Pseudomonas aeruginosa
- Meropenem/vaborbactam had acceptable EA/CA/VME/ME/MinE except for non-fermenters
- Tigecycline had acceptable EA/CA/VME/ME/MinE except for Enterobacteriales, Acinetobacter, and Aeromonas

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