Introduction

The proportion of patients receiving extended-spectrum β-lactamase (ESBL)-producing Enterobacterales (ESBLEs) has increased in both hospital and nosocomial settings in the US.

- These pathogens are responsible for approximately 157,400 cases and 92,200 deaths per year.
- In addition, this increased frequency challenges the empiric treatment of various infections and may promote the use of more potent antimicrobial agents, including carbapenems.
- This scenario highlights the emergence and dissemination of Gram-negative multidrug-resistant (MDR) pathogens in recent decades, including carbapenem-resistant Enterobacterales, where treatment options are limited.

Thus, the emergence of carbapenem-resistant Enterobacterales has become a major concern for healthcare providers, as these organisms are often resistant to multiple classes of antibiotics, including carbapenems.

Materials and Methods

Bacterial organisms
- This study comprised a collection of 1,614 Enterobacterales collected from various clinical specimens from patients hospitalized at 20 medical centers in 9 US Census Divisions during 2021. Only consecutive isolates (1 per patient infection episode) responsible for documented infections according to local criteria were included.

- Bacterial identification was confirmed by standard algorithms supported by matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) analysis (Bruker Daltonics, Bremen, Germany).

Sensitivity testing
- Isolates were tested for susceptibility by broth microdilution following the Clinical and Laboratory Standards Institute (CLSI) M07 guidelines. Aztreonam broth microdilution panels were manufactured by JMI Laboratories (North Liberty, IA, USA) and contained colistin-susceptible MBL-producing Enterobacterales (strain MBL 1001) as the control.

- Quality assurance was performed by sterility checks, colony counts, and testing 50 randomly selected quality control strains. MIC interpretation was performed using CLSI breakpoints for Enterobacterales (susceptible: ≤2 mg/L; resistant: ≥4 mg/L).

- ESBL producers were presumptively defined as Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis with ceftriaxone, ceftazidime, or amoxicillin-clavulanate ≥2 mg/L.

Results

- A total of 39 (2.9%) isolates were not susceptible to the comparator agents, including carbapenems, whereas an extensively drug-resistant phenotype as defined by any isolates susceptible to ≤2 mg/L was not identified.

- SPR206 (MIC50/90, 0.06/0.12 mg/L) and meropenem (MIC50/90, 0.03/0.06 mg/L) showed the lowest activity of the comparator agents tested against the Enterobacterales isolates (Table 2).

- Similar MIC50 and MIC90 values of 0.06 and 0.12–0.5 mg/L, respectively (Table 1).

- The CRE definition was also used to define isolates as not susceptible (MIC ≥2 mg/L) and for the extended-spectrum β-lactamase (ESBL) definition (Table 1).

- Excluding these organisms, SPR206 (MIC50/90, 0.06/0.12 mg/L) and meropenem (MIC50/90, 0.03/0.06 mg/L) showed the lowest activity of the comparator agents tested against the Enterobacterales isolates (Table 2).

In vitro Activity of SPR206 and Comparator Compounds against Enterobacterales Isolates Responsible for Infections in United States Hospitals

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Enterobacterales Isolates Responsible for Infections in United States Hospitals

This study reports the activity of SPR206 against Enterobacterales from consecutive isolates (1 per patient infection episode) responsible for infections in 30 medical centers in 9 US Census Divisions during 2021. Only consecutive isolates (1 per patient infection episode) responsible for documented infections according to local criteria were included.

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- | Antimicrobial agent | MIC (mg/L) | CLSIa | Interpretation |
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<td>Imipenem</td>
<td>≤0.12</td>
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<tr>
<td>Meropenem</td>
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<td>Ceftriaxone</td>
<td>&gt;8</td>
<td>≤0.06</td>
<td>Resistant</td>
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<tr>
<td>Piperacillin-tazobactam</td>
<td>8 &gt;128</td>
<td>≤0.5</td>
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<td>Cefazidime-avibactam</td>
<td>&gt;32 &gt;16</td>
<td>0.5-32</td>
<td>Resistant</td>
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<td>Tigecycline</td>
<td>0.25/0.5</td>
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Table 2. Activity of SPR206 and comparators against ESBL, MDR, and XDR Enterobacterales

- For many carbapenem-resistant Enterobacterales, where treatment options are limited.

- SPR206 remained in vitro active against all resistant subsets, including ESBL, CRE, MDR, and XDR groups, where tested. Intrinsically resistant profiles were available.

- These data, combined with the favorable safety and tolerability profiles in Phase 1 studies, support the continued clinical advancement of SPR206.

Conclusions

- SPR206 demonstrated more potent activity than its index comparator colistin against CRE and ESBL Enterobacterales and their resistant subsets causing infections in US hospitals.

- SPR206 remained in vitro active against all resistant subsets, including ESBL, CRE, MDR, and XDR groups, where tested.

- Intrinsically resistant profiles were available.

- These data, combined with the favorable safety and tolerability profiles in Phase 1 studies, support the continued clinical advancement of SPR206.

References


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