P0154

In vitro activity of sulbactam-durlobactam against colistin-resistant and/or cefiderocol-non-susceptible, carbapenem-resistant *Acinetobacter baumannii* collected in US hospitals

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BACKGROUND

Carbapenem-resistant *A. baumannii* (CR*Ab*)

- Major cause of healthcare-associated infections
- Highly drug resistant
- High morbidity and mortality
- Lack of reliable treatment options

Sulbactam-durlobactam (SUL-DUR)

- Novel β-lactamase inhibitor combination
- SUL inhibits *A. baumannii* penicillin-binding protein 3 (PBP3)
- DUR inhibits class A, C, and D β –lactamases
- Non-inferior to colistin when combined with imipenem (IPM) in phase 3 trial
- Resistance mechanisms include:
  - metallo-β-lactamase production,
  - *ftsI* (encodes PBP3)
  - *adeJ* mutations

MATERIALS AND METHODS

- 87 CR*Ab* isolates from US
- 68 were colistin-resistant (MIC, >2 µg/mL)
- 26 were cefiderocol-non-susceptible (MIC, ≥8 µg/mL)
- 7 were both
- Whole genome sequence data evaluated for cgSNPs, β-lactamase gene content, *ftsI*, and *adeJ* gene mutations

RESULTS

Table 1. $MIC_{50/90}$ for cefiderocol-non-susceptible isolates (n=26)

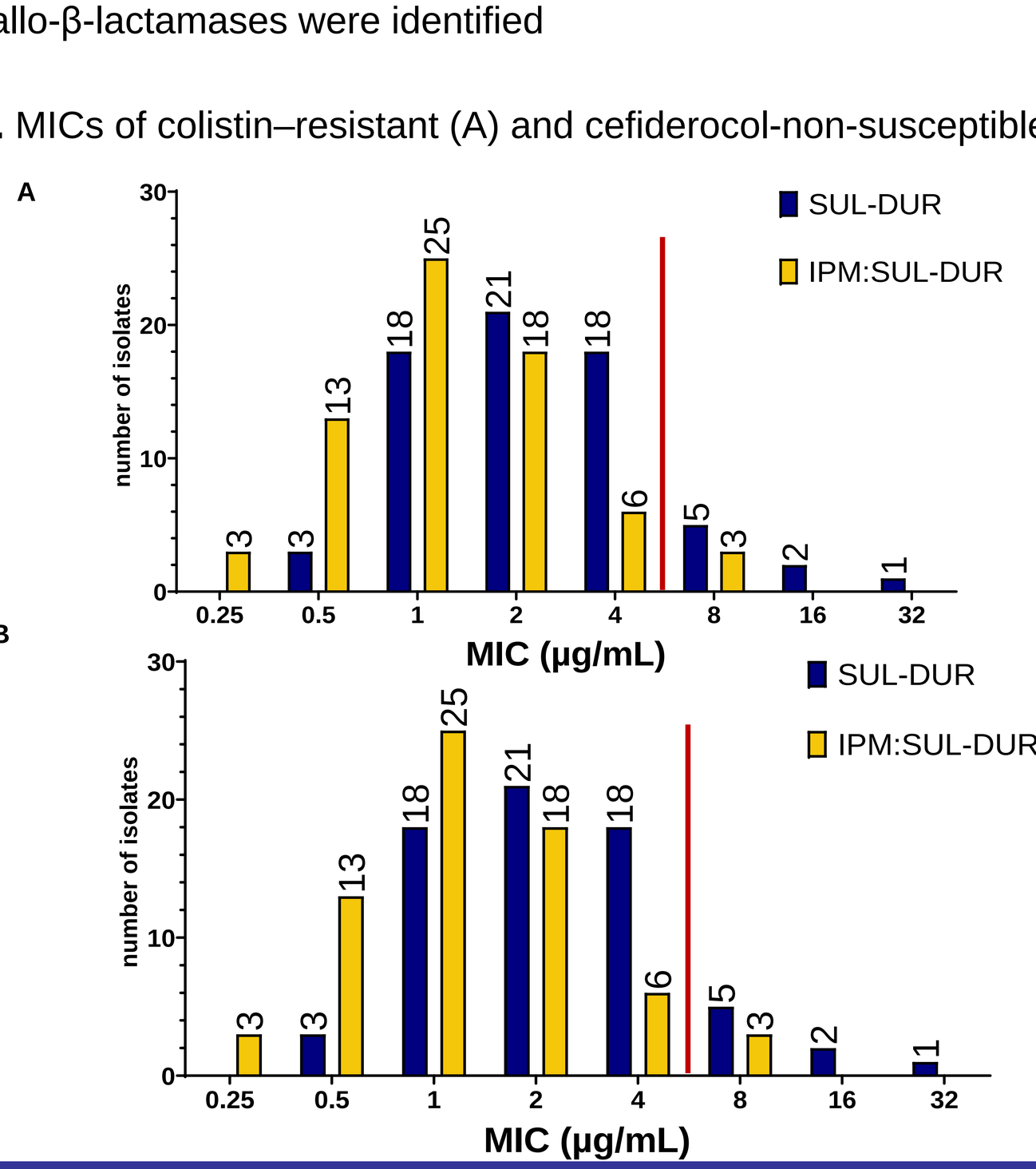
MIC (µg/mL)	IPM	SUL	SUL-DUR	IPM: SUL-DUR
Min	4	1	1	0.5
Max	64	64	16	8
MIC_{50}	32	16	4	1
MIC_{90}	64	64	8	4

Table 2. $MIC_{50/90}$ for colistin-resistant isolates (n=68)

MIC (µg/mL)	IPM	SUL	SUL-DUR	IPM: SUL-DUR
Min	4	2	0.5	0.25
Max	64	64	32	8
MIC_{50}	32	8	2	1
MIC_{90}	64	32	8	4

- 10 isolates were resistant to SUL-DUR; 3 to IPM:SUL-DUR
- Genetically diverse: **cgSNPs of 1052** (range, 0 to 46634)
- PBP3 substitutions identified among the isolates: **Y196S, V346A, H370Y, K389E, T511S, A515V, T526S**, and **F548I**
- PBP3 substitutions were more common in SUL-DUR-resistant isolates however also present in susceptible isolates
  (5/10 [50%] vs 6/77 [8%]; *p*= 0.002)
- *adeJ* mutations were identified in two isolates, one resistant, another susceptible
- No metallo-β-lactamases were identified

Figure 1. MICs of colistin–resistant (A) and cefiderocol-non-susceptible (B) isolates.



CONCLUSION

- SUL-DUR is active against majority of colistin-resistant and cefiderocol-non-susceptible CR*Ab*
- IPM further lowers MIC_{50} by 2- to 4-fold
- Additional mechanisms of resistance are present as 5/10 SUL-DUR resistant isolates did not possess known mutations

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