

Activity of Doripenem in the Context of Rising Antimicrobial Resistance in Invasive Enterobacteriaceae in the UK and Ireland

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BACKGROUND

The BSAC Bacteraemia Resistance Surveillance Programme has monitored antimicrobial resistance in organisms causing bacteraemia in the UK and Ireland since 2001.

Ertapenem and tigecycline have been tested since 2002.

Doripenem was first tested in 2005.

METHODS

Each year, 25 centres contribute up to 10 isolates each of *E. coli*, *Klebsiella* spp., *Enterobacter* spp., *Proteaeae*, and other Gram-negative bacteria from blood for central testing by the BSAC agar dilution method.

ABBREVIATIONS

CIP ciprofloxacin
GEN gentamicin
TGC tigecycline
IPM imipenem
ETP ertapenem
DOR doripenem*

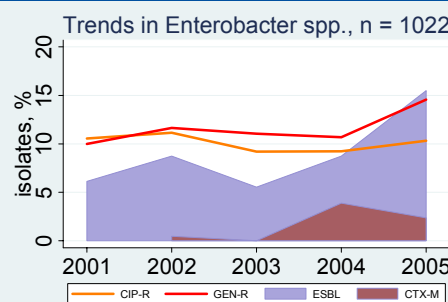
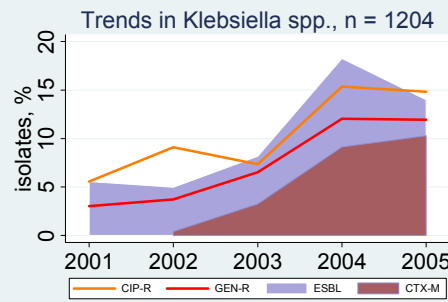
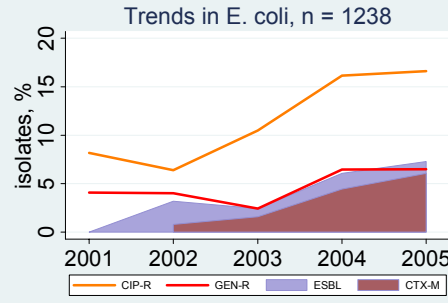
*Note: BSAC/EUCAST breakpoints have not been set for DOR with Enterobacteriaceae.

RESULTS

- ESBL production rose from low levels (0, 6 and 6%) to reach 7, 14 and 15% in *E. coli*, *Klebsiella* and *Enterobacter* respectively by 2005, but remained rare in *Proteaeae* (1/1076) and other genera (3/502).
- The rise was due to CTX-M types, now comprising 83% of ESBLs in *E. coli*, 74% in *Klebsiella* and 17% in *Enterobacter*.
- By 2005, overall CIP and GEN resistance had reached 17 and 6% in *E. coli*, 15 and 12% in *Klebsiella*, and 10 and 15% in *Enterobacter*.
- Tigecycline and carbapenems retained activity against multi-resistant isolates, although a third of ESBL-producing *Enterobacter* and *Klebsiella* were intermediate or resistant to TGC.
- Doripenem MICs were on average 8-fold lower than, and closely related to, those of imipenem.

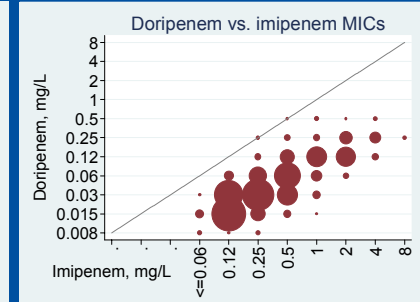
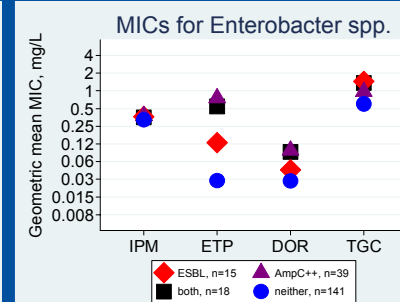
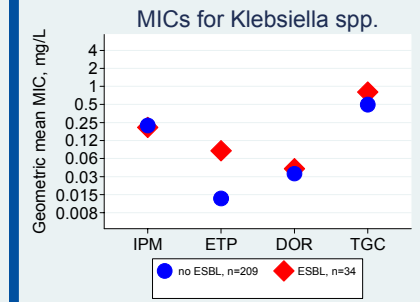
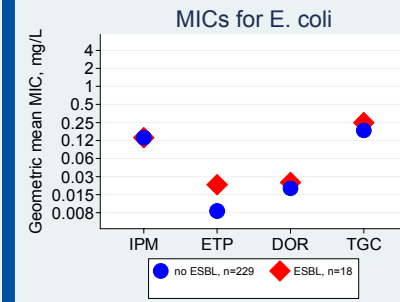
CONCLUSIONS

- The prevalence of CTX-M-producing *E. coli* and *Klebsiella* in the UK and Ireland rose sharply from 2002 to 2004.
- A notable fraction of Enterobacteriaceae here are now resistant to cephalosporins, ciprofloxacin, and gentamicin.
- Imipenem, ertapenem and doripenem differed in detail, but maintained good activity against all or most resistant isolates.



RESULTS FOR 2005

| Organism | Percentage of isolates with MICs above the level shown (mg/L) | | | | | | | | | |
|------------|---|------|-------------------|------|---------------------|------|-----------|------|--------------|------|
| | <i>E. coli</i> | | <i>Klebsiella</i> | | <i>Enterobacter</i> | | Proteaeae | | Other genera | |
| ESBL? | NON | ESBL | NON | ESBL | NON | ESBL | NON | ESBL | NON | ESBL |
| Number | 229 | 18 | 209 | 34 | 180 | 33 | 222 | 0 | 118 | 1 |
| CIP > 1 | 11 | 83 | 4 | 79 | 5 | 39 | 8 | . | 16 | . |
| GEN > 4 | 4 | 33 | 1 | 79 | 7 | 58 | 5 | . | 2 | . |
| TGC > 1 | 0 | 0 | 9 | 29 | 7 | 36 | 83 | . | 6 | . |
| ETP > 2 | 0 | 0 | 0 | 0 | 1 | 15 | 0 | . | 0 | . |
| IPM > 4 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | . | 0 | . |
| DOR* > 0.5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | . | 0 | . |



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