Poster 1361

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Activity of Cefiderocol and Comparator Agents Against Difficult-to-Treat Resistant *Acinetobacter baumannii-calcoaceticus* Complex Isolates Collected During 2020–2022 as Part of the SENTRY Antimicrobial Surveillance Program

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BACKGROUND

- Difficult-to-treat resistant (DTR) *Acinetobacter baumannii-calcoaceticus* complex shows treatment-limiting resistance to β-lactams and fluoroquinolones, and alternative treatment options are needed.
- Cefiderocol is a siderophore-conjugated cephalosporin that uses iron-uptake systems to enter the bacterium's periplasmic space.

OBJECTIVE

We aimed to determine susceptibility of cefiderocol and comparator agents against DTR *A. baumannii-calcoaceticus* complex isolates, collected in 2020–2022 in Europe and the USA as part of the SENTRY Antimicrobial Surveillance Program.

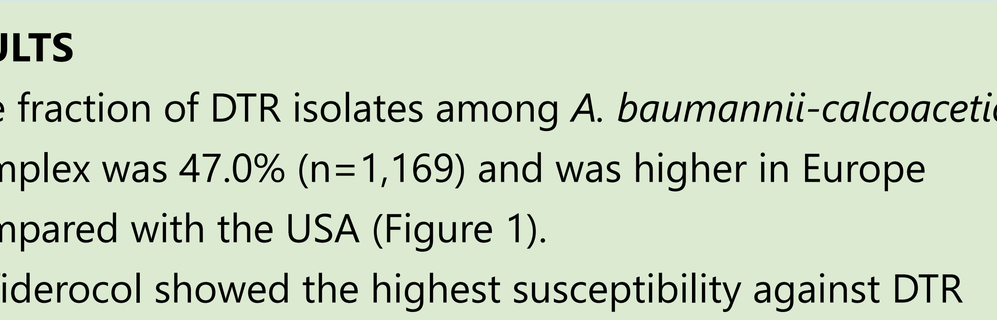
METHODS

- Minimum inhibitory concentrations were determined according to Clinical and Laboratory Standards Institute (CLSI) guidelines using broth microdilution with cation-adjusted Mueller–Hinton broth (CAMHB) for comparator agents and iron-depleted CAMHB for cefiderocol against 2,485 *A. baumannii-calcoaceticus* complex isolates collected in 2020–2022 in Europe (n=1,504) and the USA (n=981).
- Susceptibility was assessed according to European Committee on Antimicrobial Susceptibility Testing (EUCAST) pharmacokinetic/pharmacodynamic, CLSI, and US Food and Drug Administration (FDA) breakpoints.
- DTR was defined as being non-susceptible according to CLSI breakpoints to the β-lactams ceftazidime, cefepime, meropenem, imipenem, and fluoroquinolones ciprofloxacin and levofloxacin.

RESULTS

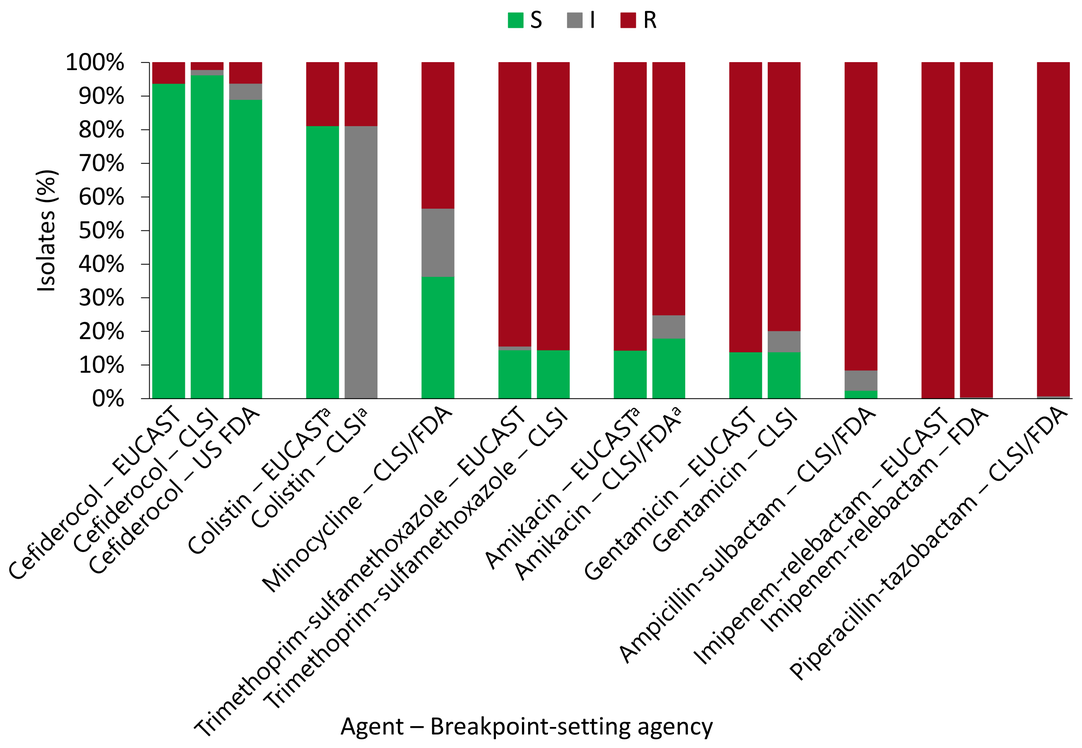
- The fraction of DTR isolates among *A. baumannii-calcoaceticus* complex was 47.0% (n=1,169) and was higher in Europe compared with the USA (Figure 1).
- Cefiderocol showed the highest susceptibility against DTR *A. baumannii-calcoaceticus* complex, with 93.8%, 96.2%, and 89.1% of the isolates susceptible according to EUCAST, CLSI, and FDA breakpoints, respectively (Figure 2).
- DTR *A. baumannii-calcoaceticus* complex isolates collected in Europe were generally less susceptible to comparator agents, compared with isolates collected in the USA, but cefiderocol showed equally good activity against both sets of isolates (Figure 3).

Figure 1: Prevalence of difficult-to-treat resistant *A. baumannii-calcoaceticus* complex in Europe (n=1,504) and the USA (n=981)



- DTR phenotype was more frequently encountered in Europe (63.2%) than in the USA (28.6%).

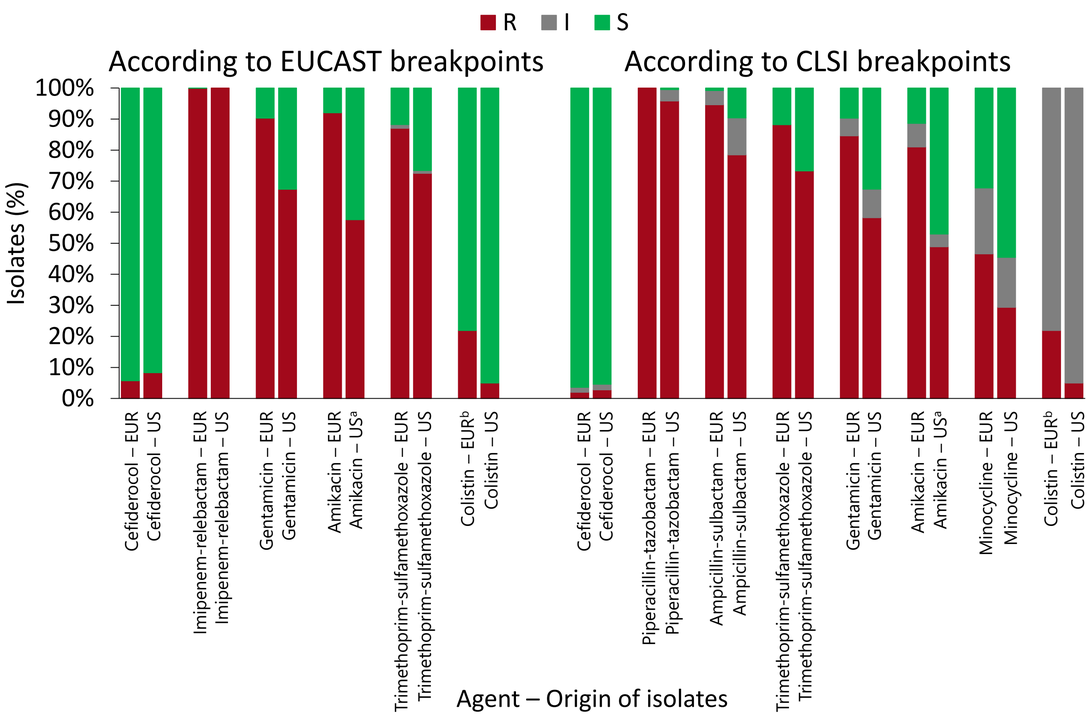
Figure 2: Susceptibility of cefiderocol and comparator agents against difficult-to-treat resistant *A. baumannii-calcoaceticus* complex (n=1,169)



- Cefiderocol showed >90% susceptibility, followed by colistin (~80%), while other agents showed much lower degrees of susceptibility (<37%).

S, susceptible; I, intermediate; R, resistant; criteria as published by CLSI (2023), EUCAST (2023), and US FDA (2023); for amikacin, only urinary tract infection breakpoints were used.
[a]One isolate was not tested (n=1168).
For systemic infections, aminoglycosides must be used in combination with other active therapy.
Colistin should not be used in monotherapy, unless used in infections where high exposure can be achieved at the site of infection (infections emanating from the urinary tract).

Figure 3: Susceptibility of cefiderocol and comparator agents against difficult-to-treat resistant *A. baumannii-calcoaceticus* complex from Europe (n=951) and the USA (n=218) using EUCAST (left) or CLSI (right) breakpoints



- Isolates from Europe were significantly more resistant to all agents compared with isolates from the USA, regardless of which breakpoints were used.
- Resistance for cefiderocol was low for isolates from both continents.

S, susceptible; I, intermediate; R, resistant; criteria as published by CLSI (2023), EUCAST (2023), and US FDA (2023); for amikacin, only urinary tract infection breakpoints were used.
[a]One isolate was not tested (n=217). [b]One isolate was not tested (n=950).
For systemic infections, aminoglycosides must be used in combination with other active therapy.
Colistin should not be used in monotherapy, unless used in infections where high exposure can be achieved at the site of infection (infections emanating from the urinary tract).

CONCLUSIONS

- DTR *A. baumannii-calcoaceticus* complex isolates from Europe were more resistant to comparator agents compared with isolates from the USA, but resistance to cefiderocol remained low for isolates from both continents.
- DTR *A. baumannii-calcoaceticus* complex isolates remained highly susceptible to cefiderocol, and cefiderocol should be considered as an early treatment option for known or suspected infections caused by these isolates.

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