In vitro activity of gepotidacin against Escherichia coli causing urinary tract infections between 2019–2021 in Europe, Russia, Israel, and Turkey, including molecularly characterized fluoroquinolone-resistant subsets

RE Mendes [1], JH Kimbrough[1], SJR Arends

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- Quality assurance was performed by sterility checks, colony counts, and testing CLSI-recommended quality control reference strains.[7] Interpretation of MIC results was performed using EUCAST criteria, except for amoxicillin-clavulanate MIC values that were interpreted using CLSI breakpoints.[7, 8]
- E. coli ZLWK 0,& UHVXOWV • PJ / IRU FLSURIOR[DFLQ DQG RU • PJ / IRU OHYRIOR[DFLQ QRW susceptible [NS] to either agent based on CLSI/EUCAST criteria) were selected for screening of fluoroquinolone resistance mechanisms. Isolates were subjected to genome sequencing, followed by screening of plasmid-mediated fluoroquinolone resistance genes and mutations in the quinolone resistance-determining regions (QRDR) of GyrA, GyrB, ParC, and ParE.

Screening of resistance determinants

Results

- A total of 24.9% (415/1,664) E. coli met the MIC criteria for screening of FQ-resistance (R) mechanisms (Table 1), and the occurrence of this phenotype was higher among isolates from Eastern European countries (35.1%) than that observed among E. coli originating from Western European countries (RI DOO).LVRODWHV
- Most FQ-NS isolates (39.0%; 162/415) had double mutations at GyrA and ParC, followed by isolates (29.9%; 124/415) with double mutations at GyrA and single mutations at ParC (Table 1).
- Among FQ-NS isolates, plasmid-mediated FQ-R genes, such as qnr variants, were detected in 11.3% (47/415) of these isolates, whereas aac-(6')-Ib-cr variants were noted in 17.8% (74/415) of isolates, including 1 strain with both genes (Table 1).
- Gepotidacin had an MIC_{50} of 2 mg/L and an MIC_{90} of 4 mg/L against both FQ-S and FQ-NS isolates (Tables 1 and 2).
- Nitrofurantoin had activity against the FQ-S and FQ-NS subsets (99.7% and 97.1%S, respectively), whereas amoxicillin-clavulanate (84.7% and 62.2% susceptible) and trimethoprim-sulfamethoxazole (79.7% and 44.4% susceptible) had limited activity (Table 2).
- Fosfomycin (91.8–98.4% susceptible) and mecillinam (91.5–98.6% susceptible) were also active (i.e., >90% susceptible) against the various E. coli subsets presented here (Table 2).
- Gepotidacin had an MIC_{50} of 1 mg/L or 2 mg/L and an MIC_{90} of 2 mg/L, 4 mg/L, or 8 mg/L against isolates with various QRDR mutations (Table 1).
- Against isolates carrying plasmid-mediated FQ-R genes, gepotidacin had MIC_{50} and MIC_{90} values of 2 mg/L and 4 mg/L against those isolates with aac-(6')-Ib-cr, whereas MIC_{50} and MIC_{90} values of 8 mg/L and 16 mg/L against the qnr subset (Table 1).

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1. Gibson EG, Bax B, Chan PF, Osheroff N. Mechanistic and Structural Basis for the Actions of the Antibacterial Gepotidacin against Staphylococcus aureus *\UDVH $&6 ,QIHFW 'LV
2. Bax BD, Chan PF, Eggleston DS, Fosberry A, Dentry DR, et al. Type IIA topoisomerase inhibition by a new class of antibacterial agents. Nature 2010;466(7309):935–940.
3. Oviatt A, et al. Poster #L0178 presented at ECCMID, 23–26 Apr, 2022, Lisbon, Portugal.
4. Biedenbach DJ, Bouchillon SK, Hackel M, Miller LA, Scangerella-Oman NE, et al. In vitro activity of gepotidacin, a novel triazaacenaphthylene bacterial topoisomerase inhibitor, against a broad spectrum of bacterial pathogens. Antimicrob Agents Chemother 2016;60(3):1918–1923.
5. Mushtaq S, et al. Poster #P1849 presented at ECCMID, 13–16 April, 2019, Amsterdam, The Netherlands.
6. Clinical and Laboratory Standards Institute (2018). M07Ed11. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Wayne, PA, USA.
s9dadmaedi sin ag dEddad vitro activity ofsrelw aer5bicallyAmsterdam, ay9):935–940.

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