In vitro activity of gepotidacin against urine isolates of *Escherichia coli* from outpatient departments in Germany, 2022/23

Gepotidacin demonstrates promising *in vitro* activity against recent *E. coli* urine isolates

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Introduction

- The major causative pathogen of community-acquired urinary tract infections (UTI) is *Escherichia coli* and acquired antimicrobial resistance has complicated effective treatments.[1, 2]
- Gepotidacin (GEP) is a novel, bactericidal, first-in-class triazaacenaphthylene antibiotic that inhibits bacterial DNA replication through a unique mechanism of action, distinct binding site and well-balanced inhibition (for most uUTI uropathogens) of 2 different Type II topoisomerases.[3]

Aims

Analyze the *in vitro* activity of gepotidacin in comparison to ciprofloxacin against a collection of *E. coli* urine isolates from outpatient departments in Germany.

Methods

- A total of 450 *E. coli* isolates collected at 23 laboratories during a surveillance study conducted by the Paul-Ehrlich-Society for Infection Therapy in 2022/23 were investigated. Susceptibility testing was performed at a reference laboratory using the broth microdilution method according to ISO 20776-1.
- EUCAST breakpoints (v.14.0) were applied to interpret the ciprofloxacin MICs. Gepotidacin breakpoints have not yet been defined. Production of extended-spectrum β-lactamases (ESBLs) was detected phenotypically via susceptibility testing and confirmed by PCR.

Results

- Three-hundred seventy (82.2%) and 80 (17.8%) isolates were obtained from female and male patients, respectively. The median (interquartile range) age of the patients was 64.5 (45.3 – 80.0) years.
- Thirty-two isolates (7.1%) produced a CTX-M-type ESBL [group 1 (n=24), group 9 (n=8)], of which 19 encoded additional beta-lactamases [TEM (n=9), OXA-1 (n=5), OXA-244 (n=1), NDM-5 (n=1), DHA (n=2), CMY (n=1)]. Seventy-six (16.9%) isolates were ciprofloxacin-resistant (including ATU), a slight increase compared to our previous study based on isolates from 2019/20 (14.8%) (Table).[4]

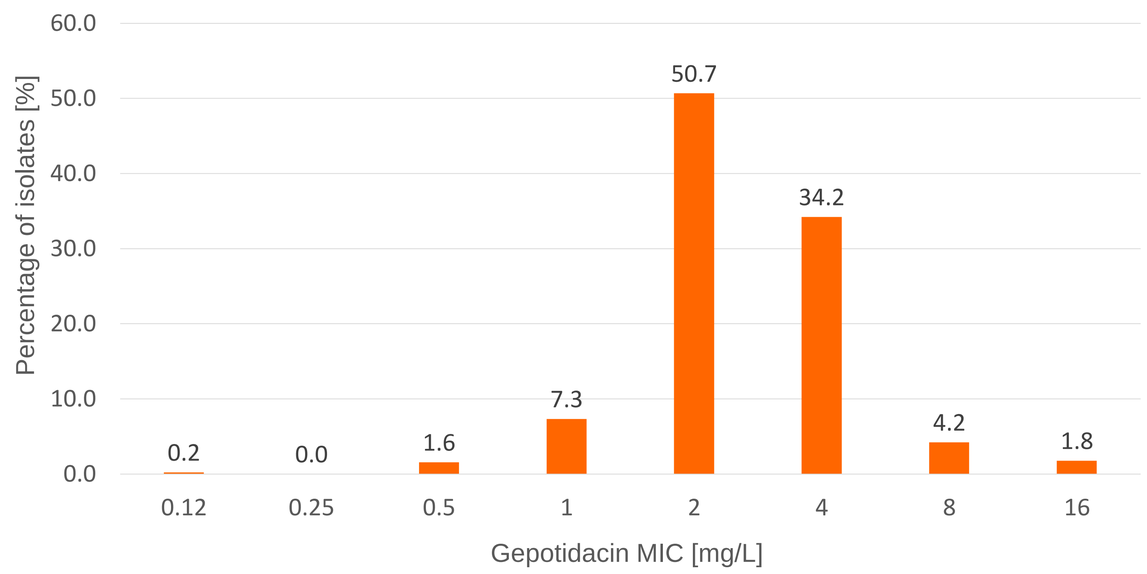
Table: MIC distributions of gepotidacin and ciprofloxacin for *E. coli* urine isolates

Phenotype / group	MIC [mg/L] ≤0.002	0.004	0.008	0.016	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	%R
All (n=450)																	
Gepotidacin							1	0	7	33	228	154	19	8			- [1]
Ciprofloxacin		3	21	230	89	5	4	22	12	2	4	58					16.9
ESBL-negative (n=418)																	
Gepotidacin							1	0	7	29	217	142	16	6			- [1]
Ciprofloxacin		3	21	225	88	5	3	20	10	1	2	40					12.7
ESBL-positive (n=32)																	
Gepotidacin							0	0	0	4	11	12	3	2			- [1]
Ciprofloxacin		0	0	5	1	0	1	2	2	1	2	18					71.9
Ciprofloxacin (S; n=374)																	
Gepotidacin							0	0	6	17	203	132	14	2			- [1]
Ciprofloxacin (ATU+R; n=76)																	
Gepotidacin							1	0	1	16	25	22	5	6			- [1]

S, isolates classified as S (susceptible at standard dose); ATU + R, isolates showing MIC values of 0.5 mg/L (ATU) and resistant isolates. We took a conservative route as per EUCAST guidance as we did not confirm MICs with a secondary testing method.; %R, percentage of resistant isolates. The underlined numbers indicate the MIC50/90 values. The solid vertical lines indicate the EUCAST breakpoint defined for ciprofloxacin resistance. Numbers in bold include isolates with MIC < value shown; numbers in italic include isolates with MIC > the highest concentration tested. [1] No EUCAST breakpoint defined.

- A slight increase in ciprofloxacin resistance was also observed in ESBL producing (71.9%) and non-producing (12.7%) isolates compared to our previous 2019/20 study [ESBL-positive (65.2%) and ESBL-negative (9.2%)].
- Overall, MIC50/90 values were 2/4 mg/L for gepotidacin and 0.016/>4 mg/L for ciprofloxacin. The gepotidacin MIC50/90 values against ESBL-producing and ciprofloxacin-resistant isolates were 4/8 mg/L and 2/8 mg/L, respectively (Table).
- The slightly higher gepotidacin MIC90s observed could be driven by low n-values in the respective subgroups. Worth noting: 4 mg/L of geptidacin inhibited 84.4% of ESBL-positive and 85.5% of ciprofloxacin-resistant isolates.
- Unimodal frequency distribution of gepotidacin MIC values (all *E. coli* isolates, n=450). MICs ranged from 0.12 – 16 mg/L with a mode of 2 mg/L (Figure).

Figure: Distribution of gepotidacin MIC values (in %) for all *Escherichia coli* isolates from urine (n=450)



Abbreviations

MIC, minimum inhibitory concentration
ATU, area of technical uncertainty
EUCAST, European Committee on Antimicrobial Susceptibility Testing

References

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Disclosures

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Conclusions

Gepotidacin continues to show promising *in vitro* activity against *E. coli* urine isolates, including ESBL-producing and ciprofloxacin-resistant isolates.

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