Fetroja® – The GAME CHANGER Trial

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Summary

- The GAME CHANGER trial was an investigator-initiated, non-inferiority, open-label study comparing cefiderocol (n=250) with SOC (n=254) antibiotics in patients with hospital-acquired or healthcare-associated BSIs caused by Gram-negative bacilli[1]
  - The study was conducted in Australia, Malaysia, Singapore, Taiwan, Thailand, and Turkey
  - The studied pathogens consisted mostly of Enterobacterales, and less frequently consisted of non-fermenters (10% *Pseudomonas* spp. and 9% *Acinetobacter* spp.)
  - 25% of patients in the GAME CHANGER trial (64 patients in the cefiderocol group and 63 patients in the SOC group) had an infection due to a CR pathogen, with approximately 50% being CRE
- The primary outcome of non-inferiority in 14-day ACM (main analysis) was met: 20 (8%) for cefiderocol and 17 (7%) for SOC; absolute risk difference (95% CI) was 1% (-3, 6), and the risk ratio (95% CI) was 1.20 (0.64, 2.23)[1]
  - The 14-day ACM in the CR subset was 9 (14%) for cefiderocol and 6 (10%) for SOC; absolute risk difference (95% CI) was 5% (-7, 16), and the risk ratio (95% CI) was 1.48 (0.56, 3.91)
    - 14-day ACM in the cefiderocol group was similar to the SOC group
    - There was insufficient evidence to reject a null hypothesis of inferiority of cefiderocol for the CR subset
    - The number of patients in the CR subset was too small to make definitive conclusions about the efficacy of cefiderocol in this subgroup
  - For patients with CR *Acinetobacter* spp. infection, the 14-day ACM was 1 (9%) for cefiderocol and 3 (21%) for SOC
- The 30-day ACM (main analysis) was 42 (17%) for cefiderocol and 38 (15%) for SOC; absolute risk difference (95% CI) was 2% (-5, 18), and the risk ratio (95% CI) was 1.12 (0.75, 1.68)[1]
  - The 30-day ACM in the CR subset was 21 (33%) for cefiderocol and 16 (25%) for SOC; absolute risk difference (95% CI) was 7% (-8, 23), and the risk ratio (95% CI) was 1.29 (0.75, 2.24)
    - For patients with CR *Acinetobacter* spp. infection, 28-day ACM was 5 (45%) for cefiderocol and 7 (50%) for SOC
- 5 treatment-emergent SAEs occurred in the cefiderocol group: abnormal liver chemistry, delirium, rash, rigors, and stupor (all considered probably or possibly related to cefiderocol)[1]
  - With the exception of rash (which required antihistamines and hydrocortisone to resolve), these AEs resolved without the need for additional treatment
  - SAEs that were considered unrelated to study drug occurred in 1 patient in the cefiderocol group (abnormal kidney function) and in 2 patients in the SOC group (both acute kidney injury)

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The GAME CHANGER Trial

The GAME CHANGER trial was an investigator-initiated, non-inferiority, open-label study comparing cefiderocol with SOC antibiotics in patients with hospital-acquired or healthcare-associated BSIs caused by Gram-negative bacilli[1]

Methods[1]

Study Design

- The study was conducted in Australia, Malaysia, Singapore, Taiwan, Thailand, and Turkey
- Patients were randomized (1:1) to receive cefiderocol (n=250) 2 g q8h, infused over 3 h, for 5–14 days or SOC (n=254) consisting of up to 3 antibiotics with activity against Gram-negative bacteria
- Key inclusion criteria included:
  - Patients ≥18 years of age
  - Positive blood culture and Gram-negative pathogen was observed on Gram stain
  - Randomization occurred within 48 h of the positive blood culture
- Key exclusion criteria included:
  - Patients with refractory shock
  - Comorbidities such that the patient's life expectancy was ≤7 days
  - BSIs that were considered related to a vascular catheter (and removal of the catheter was not possible)

Outcome Measures

- The primary outcome was 14-day ACM at a non-inferiority margin of 10%
  - If the primary outcome met the criteria for non-inferiority, a secondary analysis for superiority was conducted

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The GAME CHANGER Trial (Cont.)

Results[1]

Patient Characteristics

- Baseline characteristics were similar between the 2 treatment groups – see **Table 1**
  - The mean age of patients was 62 years for cefiderocol and 61 years for SOC
  - The median (IQR) for the CCI for both cefiderocol and SOC was 5 (3–7)
  - The median (IQR) for the SOFA score at baseline was 4 (2–6) for cefiderocol and 4 (3–7) for SOC
  - 17% and 20% of patients were in the ICU in the cefiderocol and SOC groups, respectively, at the time of randomization
  - 61% and 58% of patients in the cefiderocol and SOC group, respectively, were immunosuppressed
  - BSIs were hospital-acquired for 62% and 60% of patients in the cefiderocol and SOC groups, respectively
- Outside of an unknown source of BSI, most patients had a UTI, IAI, line-related infection, or pneumonia source of bacteremia – see **Table 1**
- The studied pathogens consisted mostly of Enterobacterales, and less frequently consisted of non-fermenters (10% *Pseudomonas* spp. and 9% *Acinetobacter* spp.) – see **Table 2**
  - Polymicrobial infections were present in 25 (10%) and 27 (11%) of patients in the cefiderocol and SOC groups, respectively

Table 1. Baseline Characteristics and Source of BSI in the GAME CHANGER Trial[1]

	Cefiderocol (n=250)	SOC (n=254)
Age (mean), years	62	61
Female	43%	40%
BMI, median (IQR), kg/m²[a]	23 (21–27)	24 (21–27)
Admitted to ICU during randomization	17%	20%
Hospital-acquired	62%	60%
CCI, median (IQR)	5 (3–7)	5 (3–7)
SOFA score, median (IQR)	4 (2–6)	4 (3–7)
Presumed source of BSI		
UTI	18%	18%
Intraabdominal	16%	19%
Line-related	16%	21%
Pneumonia	13%	12%
Skin/soft tissue/burns	5%	4%
Other	10%	6%
Unknown	18%	20%

Table 2. Select Pathogens from Index Blood Culture[1]

	Cefiderocol (n=250)	SOC (n=254)
Escherichia coli	90 (36%)	77 (30%)
Klebsiella pneumoniae	79 (29%)	80 (31%)
Enterobacter spp.	21 (8%)	21 (8%)
Other Enterobacterales spp.[a]	33 (13%)	33 (13%)
Pseudomonas spp.[b]	24 (9%)	24 (9%)
Acinetobacter spp.[c]	25 (10%)	25 (10%)
Stenotrophomonas maltophilia	3 (2%)	3 (1%)
Other[d]	16 (7%)	12 (5)%
Polymicrobial BSI	25 (10%)	27 (11%)

Fetroja® – The GAME CHANGER Trial

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The GAME CHANGER Trial (Cont.)

Table 1. Baseline Characteristics and Source of BSI in the GAME CHANGER Trial[1]

	Cefiderocol (n=250)	SOC (n=254)
Age (mean), years	62	61
Female	43%	40%
BMI, median (IQR), kg/m^2[a]	23 (21–27)	24 (21–27)
Admitted to ICU during randomization	17%	20%
Hospital-acquired	62%	60%
CCI, median (IQR)	5 (3–7)	5 (3–7)
SOFA score, median (IQR)	4 (2–6)	4 (3–7)
Presumed source of BSI		
Urinary tract	21%	18%
Intraabdominal	16%	19%
Line-related	16%	21%
Pneumonia	13%	12%
Skin/soft tissue/burns	5%	4%
Other	10%	6%
Unknown	18%	20%

Abbreviations: BMI, body mass index; BSI, bloodstream infection; CCI, Charlson Comorbidity Index; ICU, intensive care unit; IQR, interquartile range; SOC, standard of care; SOFA, Sequential Organ Failure Assessment.
[a]BMI data were missing for 5 patients (2 in the cefiderocol group and 3 in the SOC group).
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025.

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The GAME CHANGER Trial (Cont.)

Table 2. Select Pathogens from Index Blood Culture[1]

	Cefiderocol (n=250)	SOC (n=254)
Escherichia coli	90 (36%)	77 (30%)
Klebsiella pneumoniae	73 (29%)	80 (31%)
Enterobacter spp.	19 (8%)	21 (8%)
Other Enterobacterales spp.[a]	26 (10%)	33 (13%)
Pseudomonas spp.[b]	27 (11%)	24 (9%)
Acinetobacter spp.[c]	18 (7%)	25 (10%)
Stenotrophomonas maltophilia	5 (2%)	3 (1%)
Other[d]	16 (7%)	12 (5)%
Polymicrobial BSI	25 (10%)	27 (11%)

Abbreviations: BSI, bloodstream infection; SOC, standard of care.
[a]Other Enterobacterales pathogens include *Atlantibacter hermannii*, *Citrobacter freundii*, *Citrobacter koseri*, *Citrobacter werkmanii*, *Escherichia fergusonii*, *Klebsiella oxytoca*, *Klebsiella variicola*, *Leclercia adecarboxylata*, *Morganella morganii*, *Pantoea agglomerans*, *Pantoea dispersa*, *Proteus mirabilis*, *Providencia stuartii*, *Salmonella enteritidis*, and *Serratia marcescens*.
[b]Includes *Pseudomonas aeruginosa* and *Pseudomonas putida*.
[c]Includes *Acinetobacter baumannii*, *Acinetobacter nosocomialis*, *Acinetobacter pittii*, and *Acinetobacter ursingii*.
[d]Includes *Aeromonas* spp., miscellaneous non-fermenter, and other species.
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025.

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The GAME CHANGER Trial (Cont.)

Results (Cont.)[1]

- 25% of patients in the GAME CHANGER trial (64 patients in the cefiderocol group and 63 patients in the SOC group) had an infection due to a CR pathogen, with approximately 50% being CRE, based on EUCAST breakpoints (MIC >2 mg/L)
  - Among the CR subset, there were 32/64 (50%) patients with CRE in the cefiderocol group and 32/63 (51%) patients with CRE in the SOC group – see **Table 3**
  - There were 11 (4%) patients with CR *Acinetobacter* spp. in the cefiderocol group and 14 (6%) patients in the SOC group
  - CR *Pseudomonas* spp. were observed in 8 (3%) patients each in the cefiderocol group and the SOC group
  - 57 (46%) of the 127 patients with a CR pathogen had a total of 58 MBL-producing pathogens from index blood cultures
    - Of these 58 MBL-producing pathogens, there were 34 (59%) isolates with an acquired MBL gene, most commonly NDM
    - 15 (56%) of MBL-producing Enterobacterales were resistant to cefiderocol (based on EUCAST breakpoints)
  - The most common presumed sources of bacteremia in the CR subset were pneumonia with 23% and 21%, line-related with 22% and 23%, and intra-abdominal with 16% and 19%, for cefiderocol and SOC respectively[2]

Table 3. Phenotype and Molecular Characterization of Isolates[1]

	Enterobacterales spp.		*Pseudomonas* spp.[a]		*Acinetobacter* spp.		All	
Resistance type, n (%)	Cefiderocol	SOC	Cefiderocol	SOC	Cefiderocol	SOC	Cefiderocol	SOC
CR Gram-negative bacilli							64 (26)	63 (25)
CR	32 (13)	32 (13			11 (4)	14 (6)		
Cefiderocol-resistant	12 (5)	10 (			2 (1)	0		
KPC-producers	1 (<1)	3 (1)						
OXA-48 like-producers	11 (4)	15 (6)						
MBL-producers	16 (6)	11 (4)						

- The MIC distribution of cefiderocol for the index isolates are listed in **Table 4**[2]

Table 4. MIC Distribution of Cefiderocol for Index Isolates[2]

	≤0.03	0.06	0.12	0.25		2	4	8	16	32	Total
All species											
n	52	102	143	82		0	14	8	3	4	**530**
%	10	19	27	15		4	3	2	1	1	**100**

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The GAME CHANGER Trial (Cont.)

Table 3. Phenotype and Molecular Characterization of Isolates[1]

	Enterobacterales spp.		*Pseudomonas* spp.[a]		*Acinetobacter* spp.		All	
Resistance type, n (%)	Cefiderocol	SOC	Cefiderocol	SOC	Cefiderocol	SOC	Cefiderocol	SOC
CR Gram-negative bacilli							64 (26)	63 (25)
CR	32 (13)	32 (13)	8 (3)	8 (3)	11 (4)	14 (6)		
Cefiderocol-resistant	12 (5)	10 (4)	2 (1)	0	2 (1)	0		
KPC-producers	1 (<1)	3 (1)						
OXA-48 like-producers	11 (4)	15 (6)						
MBL-producers	16 (6)	11 (4)						

Abbreviations: CR, carbapenem-resistant; KPC, *Klebsiella pneumonia* carbapenemases; MBL, metallo-β-lactamases; OXA-48, oxacillinase-48; SOC, standard of care.
[a]Of the patients with CR *Pseudomonas* infections, 7 patients in each group had *P. aeruginosa*.
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025.

Table 4. MIC Distribution of Cefiderocol for Index Isolates[2]

	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	≥32	Total
All species												
n	52	102	143	82	57	45	20	14	8	3	4	**530**
%	10	19	27	15	11	8	4	3	2	1	1	**100**

Abbreviation: MIC, minimum inhibitory concentration.
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025 (Supplementary Material).

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The GAME CHANGER Trial (Cont.)

Results (Cont.)[1]

Treatment Characteristics

- The median (IQR) treatment duration was 10 (8–15) days and 13 (9–17) days for patients in the cefiderocol and SOC groups, respectively – see **Table 5**
  - For the CR population subset, the median (IQR) treatment duration was 13 (8–15) and 14 (11–20) days for the cefiderocol and SOC groups, respectively[2]
- Overall, combination treatment was used in 18% and 25% of patients in the cefiderocol and SOC groups, respectively – see **Table 5**[1,2]
  - For the subset of patients with CR infections:[2]
    - In the cefiderocol arm, 48 (75%) patients received monotherapy and 16 (25%) received combination therapy
    - In the SOC arm, 21 (33%) patients had polymyxin-based regimens (mono- or combination therapy), 9 (14%) received carbapenem monotherapy, 5 (8%) received ceftazidime–avibactam monotherapy, and 2 (3%) received piperacillin–tazobactam monotherapy. Combination therapy was utilized in 38 (60%) of patients
- The median (IQR) amount of time that patients were randomized into the cefiderocol and SOC group from positive blood culture collection was 34 (26–44) h and 33 (24–41) h, respectively[2]

Table 5. Treatment Characteristics in the GAME CHANGER Trial (Overall)[2]

	Cefiderocol (n=250)	SOC (n=254)
Total treatment duration (days), median (IQR)	10 (8–15)	13 (9–17)
Directed therapy antibiotic regimens		
Cefiderocol monotherapy, n (%)	205 (82)	–
Cefiderocol combination therapy, n (%)	45 (18)	–
SOC combination	–	63 (25)
Carbapenem	–	88 (35)
Piperacillin–tazobactam	–	53 (21)
Extended-spectrum cephalosporin[a]	–	25 (10)
Ceftazidime–avibactam	–	6 (2)
Quinolone	–	4 (2)
Polymyxin combination therapy	–	19 (7)
Polymyxin monotherapy	–	2 (1)
Other	–	15 (6)

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The GAME CHANGER Trial (Cont.)

Table 5. Treatment Characteristics in the GAME CHANGER Trial (Overall)[2]

	Cefiderocol (n=250)	SOC (n=254)
Total treatment duration (days), median (IQR)	10 (8–15)	13 (9–17)
Directed therapy antibiotic regimens		
Cefiderocol monotherapy, n (%)	205 (82)	–
Cefiderocol combination therapy, n (%)	45 (18)	–
SOC combination	–	63 (25)
Carbapenem	–	88 (35)
Piperacillin–tazobactam	–	53 (21)
Extended-spectrum cephalosporin[a]	–	25 (10)
Ceftazidime–avibactam	–	6 (2)
Quinolone	–	4 (2)
Polymyxin combination therapy	–	19 (7)
Polymyxin monotherapy	–	2 (1)
Other	–	15 (6)

Abbreviations: IQR, interquartile range; SOC, standard of care.
[a]Cefepime, cefotaxime, ceftazidime, or ceftriaxone.
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025 (Supplementary Material).

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The GAME CHANGER Trial (Cont.)

Results (Cont.)[1]

ACM

- The primary outcome of non-inferiority in 14-day ACM (main analysis) was met: 20 (8%) for cefiderocol and 17 (7%) for SOC; absolute risk difference (95% CI) was 1% (-3, 6), and the risk ratio (95% CI) was 1.20 (0.64, 2.23) – see **Table 6**
  - Secondary analysis of superiority was not achieved
- The 14-day ACM in the CR subset was 9 (14%) for cefiderocol and 6 (10%) for SOC; absolute risk difference (95% CI) was 5% (-7, 16), and the risk ratio (95% CI) was 1.48 (0.56, 3.91) – see **Table 6**
  - 14-day ACM in the cefiderocol group was similar to the SOC group
  - There was insufficient evidence to reject a null hypothesis of inferiority of cefiderocol for the CR subset
  - The number of patients in the CR subset was too small to make definitive conclusions about the efficacy of cefiderocol in this subgroup
  - Secondary analysis of superiority was not achieved

Table 6. ACM Outcomes in the Cefiderocol and SOC Arms in the GAME CHANGER Trial[1]

			Absolute risk difference (95% CI)	Risk ratio (95% CI)
Main analysis	**Cefiderocol (n=250)**	**SOC (n=254)**		
Day 14 (primary outcome)	20 (8%)	17 (7%)	1% (–3, 6)	1.2 (0.64, 2.23)
Day 30	42 (17%)	38 (15%)	2% (–5, 8)	1.12 (0.75, 1.68)
Day 90	73 (29%)	75 (30%)	0% (–8, 8)	0.99 (0.75, 1.3)
CR subset	**Cefiderocol (n=64)**	**SOC (n=63)**		
Day 14 (primary outcome)	9 (14%)		5% (–7, 16)	1.48 (0.56, 3.91)
Day 30	21 (33%)		7% (–8, 23)	1.29 (0.75, 2.24)
Day 90	31 (48%		1% (–17, 18)	1.02 (0.71, 1.46)
CR *Acinetobacter* spp. subset	**Cefiderocol (n=11)**			
Day 14 (primary outcome)	1 (9%)		–12% (–40, 15)	0.42 (0.05, 3.54)
Day 28	5 (45%)	7 (50%)	Not provided	Not provided
MBL-producing Enterobacterales	**Cefiderocol (n=16)**	**SOC (n=11)**		
Day 14 (primary outcome)	5 (31%)	0	Not provided	Not provided
Day 30	8 (50%)	2 (18%)	Not provided	Not provided

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The GAME CHANGER Trial (Cont.)

Table 6. ACM Outcomes in the Cefiderocol and SOC Arms in the GAME CHANGER Trial[1]

			Absolute risk difference (95% CI)	Risk ratio (95% CI)
Main analysis	**Cefiderocol (n=250)**	**SOC (n=254)**		
Day 14 (primary outcome)	20 (8%)	17 (7%)	1% (–3, 6)	1.2 (0.64, 2.23)
Day 30	42 (17%)	38 (15%)	2% (–5, 8)	1.12 (0.75, 1.68)
Day 90	73 (29%)	75 (30%)	0% (–8, 8)	0.99 (0.75, 1.3)
CR subset	**Cefiderocol (n=64)**	**SOC (n=63)**		
Day 14 (primary outcome)	9 (14%)	6 (10%)	5% (–7, 16)	1.48 (0.56, 3.91)
Day 30	21 (33%)	16 (25%)	7% (–8, 23)	1.29 (0.75, 2.24)
Day 90	31 (48%)	30 (48%)	1% (–17, 18)	1.02 (0.71, 1.46)
CR *Acinetobacter* spp. subset	**Cefiderocol (n=11)**	**SOC (n=14)**		
Day 14 (primary outcome)	1 (9%)	3 (21%)	–12% (–40, 15)	0.42 (0.05, 3.54)
Day 28	5 (45%)	7 (50%)	Not provided	Not provided
MBL-producing Enterobacterales	**Cefiderocol (n=16)**	**SOC (n=11)**		
Day 14 (primary outcome)	5 (31%)	0	Not provided	Not provided
Day 30	8 (50%)	2 (18%)	Not provided	Not provided

Abbreviations: ACM, all-cause mortality; CI, confidence interval; CR, carbapenem-resistant; SOC, standard of care.
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025.

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The GAME CHANGER Trial (Cont.)

Results (Cont.)[1]

Additional Outcomes

- In the main analysis, the incidence was similar between the 2 treatment groups with regards to clinical or microbiological failure (Day 14), microbiological failure (Days 3 to 90), and time to hospital discharge for patients that were alive at discharge – see **Appendix Table 1** and **Appendix Table 2**

Safety

- 5 treatment-emergent SAEs occurred in the cefiderocol group: abnormal liver chemistry, delirium, rash, rigors, and stupor (all considered probably or possibly related to cefiderocol)
  - With the exception of rash (which required antihistamines and hydrocortisone to resolve), these AEs resolved without the need for additional treatment
- SAEs that were considered unrelated to study drug occurred in 1 patient in the cefiderocol group (abnormal kidney function) and in 2 patients in the SOC group (both acute kidney injury)

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Relevant Prescribing Information

Fetroja® is indicated in patients 18 years of age or older for the treatment of:[3]

- Complicated urinary tract infections (cUTIs), including pyelonephritis caused by the following susceptible Gram-negative microorganisms:
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Proteus mirabilis*
  - *Pseudomonas aeruginosa*
  - *Enterobacter cloacae* complex
- Hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP), caused by the following susceptible Gram-negative microorganisms:
  - *Acinetobacter baumannii* complex
  - *Escherichia coli*
  - *Enterobacter cloacae* complex
  - *Klebsiella pneumoniae*
  - *Pseudomonas aeruginosa*
  - *Serratia marcescens*

Fetroja is contraindicated in:[3]

- Patients with a known history of severe hypersensitivity to cefiderocol or other beta-lactam antibacterial drugs, or any other component of **Fetroja**

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Abbreviations

ACM	all-cause mortality	ICU	intensive care unit
AE	adverse event	IQR	interquartile range
BMI	body mass index	KPC	*Klebsiella pneumonia* carbapenemase
BSI	bloodstream infection	MBL	metallo-β-lactamases
CCI	Charlson Comorbidity Index	MIC	minimum inhibitory concentration
CI	confidence interval	NA	not applicable
CR	carbapenem-resistant	NDM	New Delhi metallo-β-lactamase
CRE	carbapenem-resistance Enterobacterales	OXA-48	oxacillinase-48
cUTI	complicated urinary tract infection	Q	quartile
EUCAST	European Committee on Antimicrobial Susceptibility Testing	q8h	every 8 hours
FDA	US Food and Drug Administration	SAE	serious adverse event
g	grams	SOC	standard of care
h	hours	SOFA	Sequential Organ Failure Assessment
HABP	hospital-acquired bacterial pneumonia	UTI	urinary tract infection
IAI	intraabdominal infection	VABP	ventilator-associated bacterial pneumonia

References

1. Paterson DL, Sulaiman H, Liu P-Y, et al. Cefiderocol versus standard therapy for hospital-acquired and health-care-associated Gram-negative bacterial bloodstream infection (the GAME CHANGER trial): an open-label, parallel-group, randomized trial [Published online ahead of print]. *Lancet Infect Dis*. 2025;Oct 6. [Web Link]
2. Paterson DL, Sulaiman H, Liu P-Y, et al. Cefiderocol versus standard therapy for hospital-acquired and health-care-associated Gram-negative bacterial bloodstream infection (the GAME CHANGER trial): an open-label, parallel-group, randomized trial [Published online ahead of print]. *Lancet Infect Dis*. 2025;Oct 6 (Supplementary Material). [Web Link]
3. Fetroja® (cefiderocol) for injection, for intravenous use [Prescribing Information]. Shionogi Inc.

Enclosure

Fetroja® (cefiderocol) for injection, for intravenous use [Prescribing Information]. Shionogi Inc.

This medical response contains information in addition to that provided in the Fetroja® (cefiderocol) for injection, for intravenous use Full Prescribing Information approved by the US Food and Drug Administration (FDA). Shionogi does not recommend the use of Fetroja in any manner other than as described in the Full Prescribing Information. **Please read the attached Fetroja Full Prescribing Information.**

Appendices

Appendix Table 1. Select Secondary Outcomes (Overall Population)[1]

	Cefiderocol (n=250)	SOC (n=254)	Absolute risk difference (95% CI)
Clinical or microbiological failure by Day 14	84 (34%)	96 (38%)	–4% (–13, 4)
Clinical failure	58 (23%)	70 (28%)	–
Microbiological failure (Days 3–14)	20 (8%)	17 (7%)	–
Microbiological failure (Days 3–90)	32 (13%)	32 (13%)	0% (–6, 6)
Day of first discharge alive, median (IQR)	16 (10, 55)	19 (11, NA[a])	1.11 (0.91, 1.35)[b]

Abbreviations: CI, confidence interval; NA, not applicable; SOC, standard of care.
[a]NA because >75% of patients were discharged alive by Day 90.
[b]Sub-hazard ratio.
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025.

Appendix Table 2. Select Secondary Outcomes (CR Subset)[2]

	Cefiderocol (n=64)	SOC (n=63)	Absolute risk difference (95% CI)
Clinical or microbiological failure by Day 14	29 (45%)	34 (54%)	–9% (–26, 9)
Clinical failure	19 (30%)	24 (38%)	–
Microbiological failure (Days 3–14)	7 (11%)	10 (16%)	–
Microbiological failure (Days 3–90)	8 (12%)	14 (22%)	–10% (–23, 3)
Day of first discharge alive, median (Q1, Q3)	37 (14, NA)	30 (15, NA)	1 (0.64, 1.55)[a]

Abbreviations: CI, confidence interval; CR, carbapenem-resistant; NA, not applicable; Q, quartile; SOC, standard of care.
[a]Sub-hazard ratio.
Table adapted from Paterson et al. *Lancet Infect Dis*. 2025 (Supplementary Material).