Journal of Antimicrobial Chemotherapy

*J Antimicrob Chemother* 2021; **76**: 206–211
doi:10.1093/jac/dkaa411 Advance Access publication 29 September 2020

# Intravenous mecillinam compared with other β-lactams as targeted treatment for *Escherichia coli* or *Klebsiella* spp. bacteraemia with urinary tract focus

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*Received 2 April 2020; accepted 1 September 2020*

**Background:** Mecillinam (amdinocillin) is active against Gram-negative bacteria. Clinical data on the efficacy of IV mecillinam for severe urinary tract infections is sparse.

**Objectives:** To assess the effectiveness of targeted IV mecillinam compared with other β-lactams for bacteraemia with *Escherichia coli* and *Klebsiella* spp. and a urinary tract focus.

**Patients and methods:** We performed a retrospective cohort study at five university hospitals in the Capital Region of Denmark from 1 January 2012 to 31 December 2017. We used Cox proportional hazard regression to compare the primary composite endpoint (all-cause mortality or bacteraemia recurrence within 30 days) between patients treated with mecillinam versus ampicillin, cefuroxime, piperacillin/tazobactam and meropenem.

**Results:** We included 1129 patients in the primary analysis, of which 146 were given IV mecillinam as targeted treatment. We found no significant difference in the primary endpoint between patients treated with mecillinam versus ampicillin and cefuroxime, but found a higher risk for the primary endpoint in the piperacillin/tazobactam and meropenem groups, with adjusted HRs of 2.22 (95% CI 1.24–3.97, $P<0.01$) and 2.48 (95% CI 1.04–5.93, $P=0.04$), respectively, compared with mecillinam.

**Conclusions:** The results of this study suggest that IV mecillinam may be a suitable targeted treatment for bacteraemia with a urinary tract focus. However, these results need confirmation by randomized controlled studies.

## Introduction

Mecillinam (amdinocillin) is a penicillin derivative developed in 1972 and has activity against Gram-negative bacteria. The oral prodrug pivmecillinam is used as a first-line treatment for uncomplicated urinary tract infection in the Nordic countries and resistance has largely remained low.[1,2] In Denmark, the IV mecillinam formulation is licensed and used in severe urinary tract infections.[3] However, clinical data on the efficacy of IV treatment with mecillinam is sparse. The existing studies are mainly small studies from the 1980s or they evaluate IV mecillinam in combination with other β-lactams, most often ampicillin.[4]

In 2012, as a part of an antibiotic stewardship programme,[5] several Copenhagen hospitals introduced IV treatment with mecillinam as a targeted treatment regimen for bacteraemia with *Escherichia coli* or *Klebsiella* spp. with a urinary tract focus. The indication is limited to patients without complicating factors such as severe acute illness requiring intensive care treatment, or a complicated focus such as abscesses. The aim of this study was to assess the efficacy of this targeted treatment approach with IV mecillinam compared with other β-lactams for bacteraemia with *E. coli* or *Klebsiella* spp. and a urinary tract focus. We conducted a retrospective cohort study with a primary endpoint, consisting of the composite of all-cause mortality or recurrence of the bacteraemia within 30 days.

## Patients and methods

### Study design and setting

We performed a retrospective cohort study at five university hospitals in the Capital Region of Denmark, which corresponds to a catchment area of approximately 1.8 million inhabitants. The study period ranged from 1 January 2012 to 31 December 2017. Blood cultures were analysed at the Departments of Clinical Microbiology (DCMs), Copenhagen University Hospitals, Hvidovre and Herlev.

### Treatment regimens

The regional recommendation for empirical treatment of suspected urosepsis during the study period was either ampicillin 2 g q6h + gentamicin 5 mg/kg q24h or monotherapy with piperacillin/tazobactam 4 g/0.5g q8h. Cefuroxime 1.5 g q8h was recommended for patients allergic to penicillins. Recommendations for targeted treatment were dependent on susceptibility pattern. For ampicillin-resistant mecillinam-susceptible isolates, mecillinam 1 g q8h was introduced as an alternative to piperacillin/tazobactam, as part of an antibiotic stewardship programme to reduce the use of piperacillin/tazobactam. The indication for mecillinam is limited to patients without complicating factors such as severe acute illness requiring intensive care treatment or a complicated focus such as abscesses. Treatment recommendations include switching to oral treatment for patients with good treatment response after 2–5 days.

### Data collection

We identified patients with bacteraemia from the laboratory information system (ADBakt, Autonik, Sweden) at the DCMs. We extracted information on the sample date, microorganism and resistance pattern for both blood cultures and urine isolates. From the National Patient Register, we retrieved information on sex, age, dates of admission and discharge, comorbidities [International Classification of Diseases, Tenth Revision (ICD-10)] and procedure codes for intensive care treatment. Data on individual antibiotic treatment and medical notes were retrieved from the electronic medical records via database searches. Date of death was retrieved from the Danish Civil Registration System. All sources were linked with the unique Civil Registration Number, which characterizes all Danish residents.

### Inclusion criteria and definitions

We included patients aged $\geq$18 years with a monomicrobial blood culture positive for *E. coli* or *Klebsiella* spp. (*Klebsiella pneumoniae* or *Klebsiella oxytoca*) and a bacteriologically verified urinary tract focus (same species in blood and urine with identical susceptibility patterns for tested antibiotics; urine isolates were included if they were obtained from 7 days before to 2 days after the date of the blood culture; $\geq 10^3$ cfu/mL was regarded as significant for *E. coli*, $\geq 10^4$ cfu/mL for *Klebsiella* spp.). Only the first episode of bacteraemia per patient was included. Exclusion criteria were: missing information about hospital admission; admission to ICU; not receiving at least 48 h of targeted IV treatment with a single β-lactam antibiotic; or antibiotic treatment started >24 h before obtaining blood cultures (Figure 1). However, patients with the possibility of complicated foci such as abscesses were not excluded, as this information was not available.

The primary outcome was the composite of all-cause mortality or recurrence of the bacteraemia within 30 days. The 30 day period started after the first 48 h of targeted treatment. Recurrence was defined as bacteraemia with the same species and susceptibility pattern as the index infection, apart from the β-lactam used as the targeted treatment for the index infection. Empirical treatment was defined as treatment starting <24 h before obtaining the blood culture until the time when the final microbiological report was available. The primary empirical β-lactam was defined as the β-lactam that the patient received for the longest period during the empirical treatment. We defined targeted IV treatment as treatment started or continued after the final microbiological report was available. The time to the first dose of appropriate antibiotic was defined as the time from obtaining the blood culture until administration of the first dose of any antibiotic that the bacterium was tested as susceptible to. Nosocomial infection was defined as positive blood cultures obtained >48 h after admission. Charlson comorbidity index was calculated from the diagnostic codes obtained from any hospital admission or outpatient visit within the last 5 years of the admission with the positive blood culture.[6] The primary hospital department during the bacteraemia episode was defined as the department in which the patient had stayed the longest from blood culture until 14 days after blood culture. For a subgroup of patients where the medical notes were available, we retrieved information on blood pressure, body temperature and mental status, via text mining, and calculated and adjusted for a simplified version of the Pitt bacteraemia score (s-PBS).[7] We used the following criteria for calculation of s-PBS. Body temperature: 36.1°C–38.9°C, 0 points; 35.1°C–36.0°C or 39.0°C–39.9°C, 1 point; $\leq$35°C or $\geq$40°C, 2 points. Systolic blood pressure: <90 mmHg, 2 points. For mental status: alert, 0 points; disoriented, 1 point; stuporous, 2 points; and comatose, 4 points. If mental status was not mentioned in the medical notes, we assumed that the patient was alert. We did not extract information on cardiac arrest or mechanical ventilation, as these patients would have been excluded due to intensive care treatment. All criteria were graded within 48 h before and 24 h after obtaining the blood culture. The highest s-PBS during this period was recorded. A cut-off of PBS $\leq$3 as opposed to >3 has been used to classify critically ill patients.[8] As patients admitted to the ICU were excluded from the study, the score was used as a categorical variable for statistical analysis, with five levels (0, 1, 2, 3 and >3).

### Microbiological data

Species identification of blood isolates was performed by MALDI-TOF (Biotyper, Bruker, Bremen, Germany) and susceptibility testing was performed using the EUCAST disc diffusion method (http://www.eucast.org/ast_of_bacteria/disk_diffusion_methodology/). EUCAST mecillinam breakpoints (http://www.eucast.org/clinical_breakpoints/) for Enterobacterales are limited for uncomplicated urinary tract infection and both MIC breakpoints (S $\leq$ 8; R > 8 mg/L) and zone diameter breakpoints (S $\geq$ 15; R < 15 mm) are given. Based on pharmacokinetic/pharmacodynamic data,[9] for the indication of bacteraemic urinary tract infection, a breakpoint of S $\geq$ 20 and R < 20 mm (corresponding to an MIC breakpoint of S $\leq$ 1 and R > 1 mg/L) was used. Isolates were screened for ESBL production with cefpodoxime discs and ESBL production was confirmed by combination disc testing (Neo-Sensitabs from ROSCO Diagnostica, Taastrup, Denmark or AmpC & ESBL Detection Set from MAST, Bootle, UK). MDR was defined as resistance to third-generation cephalosporins, ciprofloxacin and gentamicin.

### Statistical analysis

Description of the cohort population characteristics included medians, IQRs and frequency tables. Comparison of categorical variables was done using the $\chi^2$ test or Fisher's exact test, as appropriate, and continuous variables were compared using the SAS QUANTREG procedure. Event-free survival was calculated from the end of the first 48 h of targeted treatment until death, recurrence of bacteraemia or the last day of follow-up, whichever came first. HRs were calculated using Cox proportional hazards regression analysis along with 95% CIs for clinical treatment failure with a follow-up period of 30 days. We adjusted the HR for potential confounders: sex, age, nosocomial infection, Charlson comorbidity index, ESBL production, additional targeted treatment with ciprofloxacin and/or gentamicin and time to first dose of appropriate antibiotic. We tested the model for proportionality using Schoenfeld residuals and Martingale residuals to test for

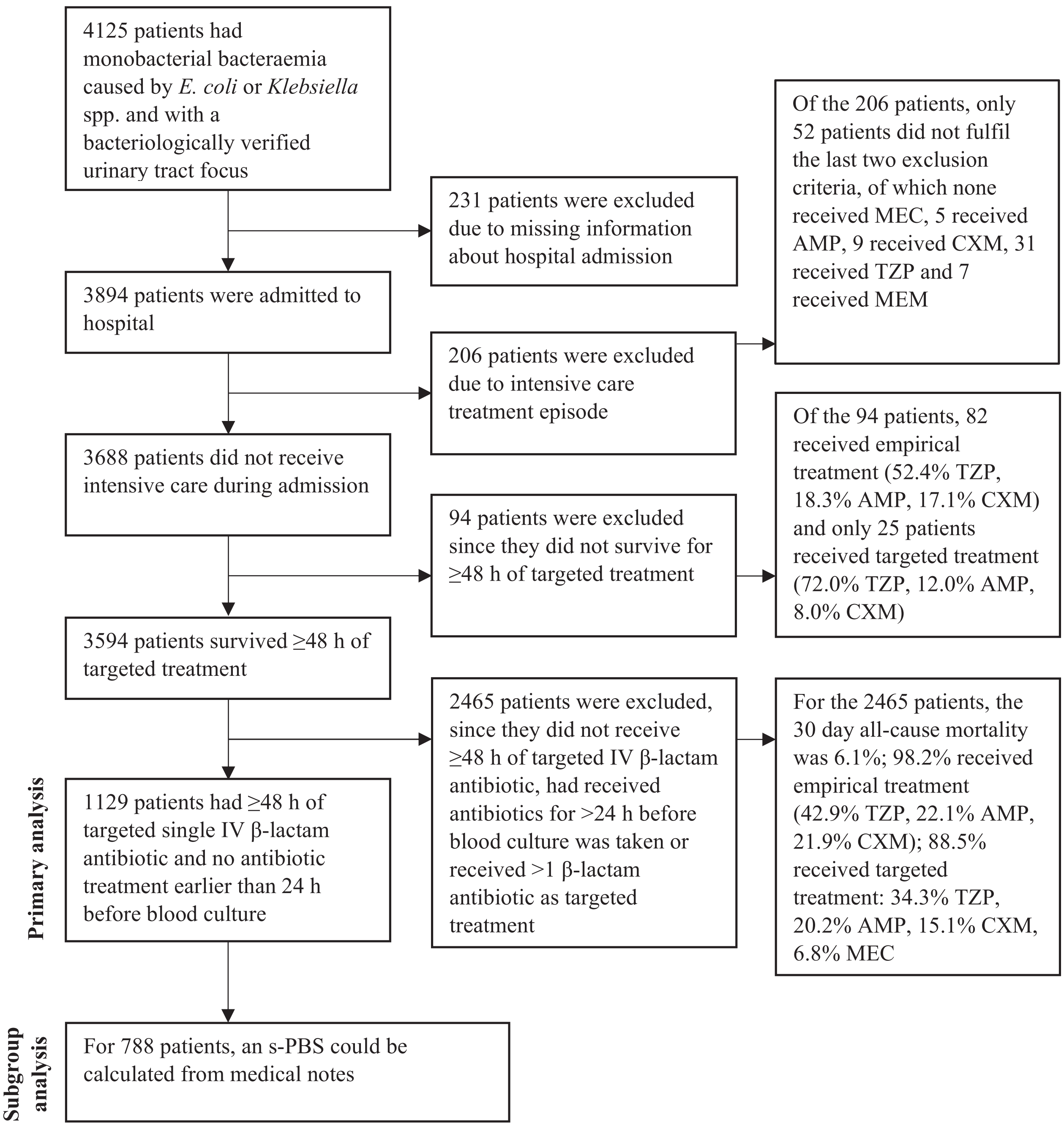


**Figure 1.** Flowchart for the inclusion of patients. AMP, ampicillin; CXM, cefuroxime; MEC, mecillinam; MEM, meropenem; TZP, piperacillin/tazobactam.

linearity of the continuous variables (age and time to first dose of appropriate antibiotic). We performed a subgroup analysis on patients where the s-PBS was available to study whether adjusting for the severity of the acute illness would impact the estimates for HRs. All analysis was performed in SAS 9.4.

### *Ethics*

The study was approved by the Danish Patient Safety Authority (Record no. 3-3013-2248/1) and the Danish Data Protection Agency (Record no. HGH-2017-128).

## Results

We identified 4125 patients with monobacterial bacteraemia caused by *E. coli* or *Klebsiella* spp. and with a bacteriologically verified urinary tract focus. Of these, 1129 were included in the primary analysis and 788 in the subgroup analysis where we adjusted for severity of the acute illness with the s-PBS (Figure 1).

The characteristics of the study population are presented in Table 1. The median age for the total population was 77 years (IQR 67–84). Compared with the mecillinam group, patients in the

**Table 1.** Characteristics of the study population

| Characteristic | Mecillinam | Ampicillin | Cefuroxime | Piperacillin/ tazobactam | Meropenem |
|---|---|---|---|---|---|
| *n* (total = 1129) | 146 | 173 | 231 | 508 | 71 |
| Age (years), median (IQR) | 78 (68–85) | 78 (68–86) | 78 (66–86) | 76 (67–83) | 72 (66–82)[a] |
| Sex, female | 72 (49.3) | 91 (52.6) | 118 (51.1) | 276 (54.3) | 26 (36.6) |
| Charlson comorbidity index | | | | | |
| 0 | 43 (29.5) | 65 (37.6) | 69 (29.9) | 133 (26.2) | 18 (25.4) |
| 1–2 | 24 (16.4) | 28 (16.2) | 45 (19.5) | 83 (16.3) | 14 (19.7) |
| >2 | 79 (54.1) | 80 (46.2) | 117 (50.7) | 292 (57.5) | 39 (54.9) |
| Speciality | | | | | |
| internal medicine | 109 (74.7) | 142 (82.1) | 189 (81.8) | 341 (67.1) | 46 (64.8) |
| abdominal surgery | 2 (1.4) | 2 (1.2) | 4 (1.7) | 29 (5.7) | 1 (1.4) |
| other surgery | 4 (2.7) | 4 (2.3) | 12 (5.2) | 19 (3.7) | 2 (2.8) |
| haematology/oncology | 9 (6.2) | 3 (1.7) | 5 (2.2) | 38 (7.5) | 5 (7.0) |
| nephrology | 3 (2.1) | 1 (0.6) | 1 (0.4) | 14 (2.8) | 6 (8.5) |
| urology | 19 (13.0) | 21 (12.1) | 20 (8.7) | 67 (13.2) | 11 (15.5) |
| Nosocomial infection | 10 (6.9) | 9 (5.2) | 19 (8.2) | 67 (13.2)[a] | 11 (15.5)[a] |
| *Klebsiella* spp. | 33 (22.6) | 0 (0)[a] | 34 (14.7) | 121 (23.8) | 10 (14.1) |
| ESBL-producing isolates | 4 (2.7) | 0 (0)[a] | 0 (0)[a] | 36 (7.1) | 33 (46.5)[a] |
| MDR isolates | 4 (2.7) | 0 (0)[a] | 0 (0)[a] | 12 (2.4) | 21 (29.6)[a] |
| Resistant to | | | | | |
| MEC | 0 (0) | 0 (0) | 30 (13.0) | 45 (8.9) | 10 (14.1) |
| AMP | 127 (87.0) | 0 (0) | 136 (58.9) | 388 (76.4) | 54 (76.1) |
| CXM | 8 (5.5) | 0 (0) | 0 (0) | 39 (7.7) | 38 (53.5) |
| TZP | 4 (2.7) | 0 (0) | 20 (8.7) | 0 (0) | 15 (21.1) |
| MEM | 0 (0) | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| Primary empirical β-lactam treatment, top three (%) | | | | | |
| 1st | AMP (47.6) | TZP (53.3) | CXM (80.0) | TZP (73.3) | CXM (31.0) |
| 2nd | TZP (26.2) | AMP (33.7) | TZP (4.8) | AMP (11.7) | MEM (29.6) |
| 3rd | MEC (9.0) | CXM (7.7) | AMP (4.8) | CXM (5.0) | TZP (19.7) |
| Time to appropriate treatment (h), median (IQR) | 6.6 (2.5–16.2) | 4.0 (1.6–10.3)[a] | 5.5 (2.3–14.5) | 4.9 (1.9–12.8) | 10.1 (1.6–40.9) |
| Additional gentamicin treatment, targeted | 5 (3.4) | 11 (6.4) | 13 (5.6) | 17 (3.4) | 0 (0) |
| Additional ciprofloxacin treatment, targeted | 1 (0.7) | 2 (1.2) | 58 (25.1)[a] | 62 (12.2)[a] | 12 (16.9)[a] |
| *Clostridioides difficile* infection within 60 days | 4 (2.7) | 3 (1.7) | 12 (5.2) | 17 (3.4) | 5 (7.0) |
| Recurrence of bacteraemia within 30 days | 7 (4.8) | 3 (1.7) | 4 (1.7) | 18 (3.5) | 5 (7.0) |
| 30 day all-cause mortality | 6 (4.1) | 16 (9.3) | 15 (6.5) | 71 (14.0)[a] | 7 (9.9) |
| Primary endpoint (composite) | 13 (8.9) | 18 (10.4) | 19 (8.2) | 88 (17.3)[a] | 11 (15.5) |

All values are *n* (%), unless otherwise stated. AMP, ampicillin; CXM, cefuroxime; MEC, mecillinam; MEM, meropenem; TZP, piperacillin/tazobactam.
[a]$P < 0.05$ when compared with the mecillinam group.



meropenem group were significantly younger. The proportion of women was 51.6% and there was no significant difference between the mecillinam group and the four other groups ($P = 0.08$). Fifty-four percent of the patients had a Charlson comorbidity index >2 and this percentage did not vary significantly between the patient groups treated with the different β-lactam antibiotics ($P = 0.20$). Most patients were admitted to internal medicine departments (73.3%). Ten percent of the patients had a nosocomial infection and both the piperacillin/tazobactam group and the meropenem group had a significantly higher proportion of nosocomial infections compared with the mecillinam group ($P = 0.04$ and $P = 0.04$, respectively). The overall resistance to the five β-lactams was 7.5% for mecillinam, 62.4% for ampicillin, 3.5% for piperacillin/tazobactam, 7.5% for cefuroxime and 0% for meropenem. There were differences in the primary empirical β-lactam treatment (as mono- or combination therapy) between the five groups, but overall piperacillin/tazobactam was the primary choice with which 46.3% of all patients were treated, followed by cefuroxime (22.6%) and ampicillin (17.7%). The median time to first appropriate dose of antibiotic was 5.1 h (IQR 2.0–14.2) and was significantly shorter in patients treated with ampicillin than in the mecillinam group ($P = 0.04$). The overall recurrence of the bacteraemia was 3.2%. The overall 30 day all-cause mortality was 10.2% and was significantly higher in the piperacillin/tazobactam group compared with the mecillinam group (14.0% versus 4.1%; $P < 0.01$).

The Cox regression analysis for the primary endpoint showed a significant difference between mecillinam versus piperacillin/tazobactam and between mecillinam versus meropenem, favouring

**Table 2.** Multivariate Cox regression analysis for the HR of the primary endpoint (composite of all-cause mortality or recurrence of bacteraemia within 30 days), stratified by targeted antibiotic treatment

| | Crude | | Adjusted[a] | |
|---|---|---|---|---|
| Treatment | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Mecillinam | Ref | — | Ref | — |
| Ampicillin | 1.17 (0.58–2.37) | 0.66 | 1.19 (0.58–2.42) | 0.64 |
| Cefuroxime | 0.92 (0.46–1.86) | 0.81 | 1.01 (0.50–2.05) | 0.99 |
| Piperacillin/ tazobactam | 1.98 (1.11–3.52) | 0.02 | 2.22 (1.24–3.97) | <0.01 |
| Meropenem | 1.81 (0.82–4.01) | 0.14 | 2.48 (1.04–5.93) | 0.04 |

Ref, reference.
[a]Adjusted for sex, age, Charlson comorbidity index, nosocomial infection, ESBL-producing isolate, additional targeted treatment with ciprofloxacin and/or gentamicin and time to first dose of appropriate antibiotic.

**Table 3.** Multivariate Cox regression analysis for the HR of the primary endpoint (composite of all-cause mortality or recurrence of bacteraemia within 30 days), stratified by targeted antibiotic treatment for the subgroup with available s-PBS

| | Crude | | Adjusted[a] | |
|---|---|---|---|---|
| Treatment | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Mecillinam | Ref | — | Ref | — |
| Ampicillin | 1.26 (0.48–3.30) | 0.63 | 1.24 (0.47–3.29) | 0.67 |
| Cefuroxime | 1.02 (0.40–2.60) | 0.97 | 1.12 (0.43–2.91) | 0.81 |
| Piperacillin/ tazobactam | 2.25 (0.99–5.09) | 0.05 | 2.60 (1.13–5.96) | 0.02 |
| Meropenem | 1.70 (0.57–5.11) | 0.35 | 1.95 (0.58–6.56) | 0.25 |

Ref, reference.
[a]Adjusted for sex, age, Charlson comorbidity index, nosocomial infection, ESBL-producing isolate, additional targeted treatment with ciprofloxacin and/or gentamicin, time to first dose of appropriate antibiotic and s-PBS.

mecillinam (Table 2). After adjusting for confounders, the HR for the piperacillin/tazobactam group was 2.22 (95% CI 1.24–3.97, $P < 0.01$) and the HR for the meropenem group was 2.48 (95% CI 1.04–5.93, $P = 0.04$), both compared with the mecillinam group.

The patient characteristics for the subgroup analysis of patients with an available s-PBS can be seen in Table S1 (available as Supplementary data at *JAC* Online). The proportion of patients with an s-PBS >3 was low (2.4%). The ampicillin group had significantly lower and the meropenem group significantly higher s-PBS than the mecillinam group (Table S1). However, there was no significant difference in the proportion of patients with an s-PBS >3 ($P = 0.97$). The Cox regression analysis of the subgroup showed that the only significant difference for the primary endpoint was observed in the piperacillin/tazobactam group compared with the mecillinam group, HR 2.60 (95% CI 1.13–5.96, $P = 0.02$) (Table 3).

## Discussion

In this retrospective study, we analysed the composite endpoint all-cause mortality or recurrence of bacteraemia within 30 days for patients with *E. coli* or *Klebsiella* spp. bacteraemia and a urinary tract focus treated with IV mecillinam versus other β-lactams. We found no significant differences, except when comparing with piperacillin/tazobactam and meropenem, which were associated with a significantly increased mortality compared with mecillinam. However, for a subgroup with adjustment for severity of acute illness using s-PBS, we only found a significant difference between mecillinam versus piperacillin/tazobactam. This suggests that IV mecillinam may be an adequate treatment for bacteraemia with urinary tract focus in non-critically ill patients.

Previous prospective studies examining IV mecillinam treatment for severe urinary tract infections mostly include older studies in small patient groups.[10–15] In these six studies a total of 159 patients received IV mecillinam, but only two studies used IV mecillinam as monotherapy with a total of 45 patients.[10,11] In the first study, mecillinam showed a lower rate of clinical cure for patients with pyelonephritis compared with the first-generation cephalosporin, cefaloridine.[10] In the second study, mecillinam showed similar clinical cure compared with trimethoprim.[11] Thus, only one previous study compared mecillinam with another β-lactam antibiotic, with only 25 patients receiving IV mecillinam.

A retrospective study reported a lower 30 day all-cause mortality rate for mecillinam compared with other antibiotics for patients with bacteraemia caused by *Klebsiella* spp.[16] However, this study pooled other antibiotics in the comparison and therefore the results are not comparable to our findings.

Our study has several strengths and limitations. We studied a real-life situation of a common condition that requires hospitalization and IV antibiotic treatment. We included a large study population compared with previous studies, even though we had restrictive inclusion criteria to ensure valuable results. Our intention was to examine targeted treatment and we therefore chose to only include patients who had received >48 h of targeted IV treatment with a single β-lactam antibiotic. In this bacteraemia population of non-critically ill patients with a urinary tract focus, which has a relatively low mortality of 10.2%, the duration of IV treatment is rather short. In contrast, we judged that ≥48 h of targeted treatment was necessary to be able to evaluate this treatment.

The main limitation of the study is its retrospective design. It is not possible to control for all differences in baseline characteristics (measured and unmeasured) that could influence choice of targeted treatment and thereby the results, e.g. confounding by indication. One factor that could influence the choice of treatment is the severity of the acute illness. The s-PBS showed significant difference between the mecillinam versus the meropenem group and between the mecillinam versus the ampicillin group. In fact, after adjustment for the severity using s-PBS in a subgroup analysis, the HR for the primary endpoint was not significantly higher in the meropenem group compared with the mecillinam group but remained significantly higher in the piperacillin/tazobactam group. To avoid confounding by indication, we defined ICU admission as an exclusion criterion, because mecillinam is not used in patients who are critically ill at presentation. However, that exclusion is also a limitation, since ICU admission is a competing risk and we do not have information on whether intensive care treatment started before or after initiation of targeted treatment.

Piperacillin/tazobactam was dosed at 4 g/0.5g q8h in this study, which corresponds to the dosage the EUCAST breakpoints are based on (https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Rationale_documents/Piperacillin-tazobactam_rationale_Nov2010_v_1.0.pdf). However, the results may be different with q6h dosing.

Only 2.3% of the patients in the subgroup analysis had an s-PBS >3, which is not surprising, as patients admitted to the ICU were excluded from the study. We used this exclusion criterion because mecillinam is not used in critically ill patients in our hospitals, in contrast to the other β-lactams, and inclusion of ICU patients thus would increase confounding by indication. However, it was not possible for us to exclude patients with complicated foci such as abscesses. In these cases, mecillinam is not recommended according to our treatment guidelines, which may lead to confounding by indication.

The oral prodrug of mecillinam, pivmecillinam, has been used in the Nordic countries for many decades and, despite that, resistance rates have remained low, although in 2017 and 2018, increasing resistance rates of 16%–17% were observed in Danish *K. pneumoniae* urine isolates,[17] which warrants close surveillance in the future. Additionally, mecillinam is mainly active against Gram-negative bacteria. Therefore, mecillinam has a favourable profile in an antibiotic stewardship context and is, in our hospitals, preferred to cephalosporins and piperacillin/tazobactam for targeted treatment of urinary tract infections with Enterobacterales.

In conclusion, patients treated with mecillinam had a similar risk of the primary endpoint compared with ampicillin and cefuroxime, and a significantly lower risk compared with piperacillin/tazobactam and meropenem, the latter not being significant after adjustment for acute illness. These results suggest that IV mecillinam may be used as targeted treatment for bacteraemia with a urinary tract focus. However, these results need confirmation by randomized controlled studies.

## Funding

This study was carried out as part of our routine work.

## Transparency declarations

None to declare.

## Supplementary data

Table S1 is available as Supplementary data at *JAC* Online.

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