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Short Communication

In vitro activity of ceftaroline against *mecC*-positive MRSA isolates

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ABSTRACT

Ceftaroline is a new cephalosporin with activity against methicillin-resistant *Staphylococcus aureus* (MRSA). A collection of 17 clinical and veterinary *mecC*-positive MRSA isolates was tested to evaluate the in vitro efficacy of ceftaroline against recently emerged *mecC*-MRSA isolates. Minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) of ceftaroline for the 17 isolates were determined by broth microdilution using the methodology and interpretive criteria of the Clinical and Laboratory Standards Institute (CLSI). Additional susceptibility tests were performed using ceftaroline M.I.C.Evaluator (M.I.C.E.TM) strips. All isolates showed susceptibility according to CLSI breakpoints, with MICs of ceftaroline ranging from 0.125 mg/L to 0.25 mg/L. MBCs were identical or up to a twofold dilution step higher. In conclusion, all tested isolates, from various sources and belonging to several clonal complexes (CCs), but predominantly to CC130, were found to be susceptible to ceftaroline. Ceftaroline could thus be an option for the treatment of *mecC*-MRSA infections.

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1. Introduction

Recently, methicillin-resistant *Staphylococcus aureus* (MRSA) strains have been described that harbour an alternative *mecA* homologue, named *mecC*, encoded on a novel type XI staphylococcal cassette chromosome *mec* (SCC*mec*) element [1,2]. The *mecC* gene (GenBank accession nos. FR823292.1, FR821779. 1:SARLGA251_00260) encodes a protein with 61.3% identity at the amino acid level to *mecA*-encoded modified penicillin binding

* Corresponding author at: Institute for Medical Microbiology and Hygiene, Technical University of Dresden, Dresden, Germany. Tel.: +49 15117166825. *E-mail address:* monecke@rocketmail.com (S. Monecke). protein 2A (PBP2A) (FR821779.1:SARLGA251_00260 vs. EMBL Y00688). The *mecC* gene have been found in association with *S. aureus* clonal complexes (CCs) 49, 130, 425, 599 and 1943 as well as in some coagulase-negative staphylococcal species. SCC*mec* XI MRSA has been identified in various European countries [3]. They can cause infections in humans [1,4], sometimes severe or fatal [5]. There are also several reports of these strains in wild and domestic animals [3,6–10], suggesting a zoonotic origin for *mecC*. Indeed, Harrison et al. [4] recently provided evidence using whole-genome sequencing supporting a zoonotic background for *mecC*-positive MRSA and zoonotic transmission.

Ceftaroline is a new cephalosporin with activity against MRSA. It has good affinity against PBP2A, therefore it can be considered as a promising therapy against infections caused by *mecA*-positive

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S. aureus. Although the in vitro activity of ceftaroline against *mecA*-MRSA has been extensively studied [11–18], to the best of our knowledge little is known of the potential efficacy of this compound against *mecC*-MRSA [19].

2. Materials and methods

In this study, 17 *mecC*-MRSA isolates were investigated. Six isolates originated from humans, five from livestock, five from

Table 1

Staphylococcus aureus isolates, strain affiliations, and ceftaroline minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values.

Isolate ID	Strain affiliation (by array hybridisation)	Presence of <i>mecA/C</i> genes (by array hybridisation)	Source	Ceftaroline MIC by BMD (mg/L)	Ceftaroline MBC (mg/L)	Ceftaroline MIC by M.I.C.E. TM strips (mg/L)
115434 (=M10-0061)	CC130-MRSA-XI	mecC	Patient isolate, from a male inpatient from the southeast of Ireland [1]	0.25	0.5	1.0
131027 (=M10-0148)	CC130-MRSA-XI	mecC	Patient isolate, from a female inpatient from Dublin, Ireland [1]	0.125	0.125	0.5–1.0 ^a
179110	CC130-MRSA-XI	mecC	Patient isolate from Brandenburg, Germany; abscess in an otherwise	0.125	0.5	0.25
201908	CC130-MRSA-XI	mecC	healthy child from a rural area Patient isolate from Brandenburg, Germany; blood culture during haematological disorder	0.25	0.5	0.5
197653	CC130-MRSA-XI	mecC	Patient isolate from Brandenburg, Germany; tracheal secretion, patient with myocardial infarction	0.25	0.25	0.5
247167	CC130-MRSA-XI	тесС	and pulmonary oedema Patient isolate from Saxony, Germany; nasal swab from a patient with malum perforans in	0.125	0.25	0.25
179029 (=V583-03)	CC130-MRSA-XI	mecC	which MRSA was detected Wildlife (hedgehog) isolate from Sweden [7]; animal with fatal septicaemia and multiple organ	0.25	0.25	0.5-1.0ª
170959 (= V5406-11)	CC130-MRSA-XI	тесС	infections Wildlife (hedgehog) isolate from the isle of Gotland, Sweden [7]; animal with severe diffuse	0.25	0.5	0.5-1.0 ^a
203236	CC130-MRSA-XI	тесС	dermatitis Wildlife (fallow deer) isolate from North Rhine-Westphalia, Germany; nasal swab of a shot	0.25	0.5	0.5–1.0 ^a
204204	CC130-MRSA-XI	mecC	animal Wildlife (fox) isolate from North Rhine-Westphalia, Germany; nasal swab of a shot animal	0.25	0.25	0.5 ^a
203344	CC130-MRSA-XI	mecC	Livestock (cattle) isolate from Bavaria, Germany; subclinical mastitis [9]	0.125	0.25	0.5–1.0 ^a
203346	CC130-MRSA-XI	mecC	Livestock (cattle) isolate from Bavaria, Germany; subclinical mastitis [9]	0.25	0.25	0.5-1.0 ^a
203353	CC130-MRSA-XI	mecC	Livestock (cattle) isolate from Bavaria, Germany; subclinical mastitis [9]	0.25	0.25	0.5
203360	CC130-MRSA-XI	mecC	Livestock (cattle) isolate from Bavaria, Germany; subclinical mastitis [9]	0.25	0.25	0.5–1.0 ^a
203364	CC130-MRSA-XI	mecC	Livestock (cattle) isolate from Bavaria, Germany; subclinical mastitis [9]	0.25	0.25	0.5
240048	CC599-MRSA-XI	mecC	Wildlife (hedgehog) isolate from Thuringia, Germany; pharyngeal swab of road-killed animal	0.125	0.125	0.25
213989	CC1943-MRSA-XI	mecC	Strain from laboratory proficiency testing programme (November 2013; courtesy of INSTAND e.V.)	0.125	0.125	0.25
136142	CC130-MSSA	mecA/C-negative	Livestock (goat or sheep) isolate from Thuringia, Germany	0.25	0.25	0.12
ATCC 25923	CC30-MSSA	<i>mecA/C</i> -negative	Laboratory control strain; patient isolate from Seattle, WA, isolated in the 1940s	0.125	0.5	0.12
ATCC 29213 ATCC 33592	CC5-MSSA ST239-MRSA-III	<i>mecA/C</i> -negative <i>mecA</i>	Laboratory control strain Laboratory control strain; patient isolate from New York, NY, around 1980	0.125 0.5	0.125 0.5	0.125 0.5

BMD, broth microdilution; M.I.C.E., M.I.C.EvaluatorTM; CC, clonal complex; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*. ^a Growth of numerous small colonies at the edge of the inhibition zone.

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