

# Activity of ceftaroline against clinically relevant strains of penicillin non-susceptible *S. pneumoniae*

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## Introduction and Purpose

Ceftaroline is a new parenteral semi-synthetic oxymino-cephalosporin. Ceftaroline exhibits activity against many gram-positive organisms including *Streptococcus pneumoniae*. Activity against penicillin resistant strains of *S. pneumoniae* has been reported. EUCAST breakpoints for *S. pneumoniae* were published in 2013 (S  $\leq$  0.25 mg/L, R > 0.25 mg/L), however, zone diameter breakpoints are missing. We wanted to examine the in-vitro activity of ceftaroline against a collection of penicillin non-susceptible *S. pneumoniae* clinical isolates (MIC  $\geq$  0.12 mg/L) and correlate them with zone diameters.

## Materials and Methods

From January 2008 until December 2012 all clinically relevant penicillin non-susceptible strains of *S. pneumoniae* (MIC  $\geq$  0.12 mg/L) were stored at -80°C for further investigations. These strains were thawed and tested for ceftaroline susceptibility using E-Test (Oxoid, 0.002-32 mg/L) and agar diffusion (Oxoid, 5 µg). All strains were tested at least twice (MH-F, bioMerieux, o/n 36°C, 5% CO<sub>2</sub>). In case of discrepancies (E-Test: more than one two-fold dilution, agar diffusion  $\geq$  2 mm) a third experiment was performed. ATCC 49619 was used as quality control.

Sex	No
Male	12
Female	11
<b>Total</b>	<b>23</b>

Table 1: Gender

material	No
blood	14
bronchoalveolar lavage	1
conjunctiva	1
mastoid	1
nose (CF)	3
tracheal secretion	3
<b>Total</b>	<b>23</b>

Table 2: Material distribution

Age (y)	No
<b>&lt;18</b>	<b>9</b>
1	4
3	1
5	2
8	1
9	1
<b><math>\geq</math>18</b>	<b>14</b>
45	1
46	1
60	2
63	1
66	1
69	3
73	1
74	3
87	1

Table 3: Age distribution

## Results

- 23 different penicillin non-susceptible *S. pneumoniae* strains could be identified.
- MIC for penicillin ranged from 0.12-4 mg/L. 9 strains originated from patients <18, 14 from patients  $\geq$ 18. 12 patients were male, 11 were female. The most common serotypes were 19A (7 strains) and 23B (5 strains).
- Most of the strains were isolated from blood culture (14 strains).
- MIC for ceftaroline ranged between 0.008 and 0.25 mg/L.
- Zone diameters ranged between 28 and 42 mm.

Serotype	No
15A	2
15B	2
16F	1
19A	7
19F	2
23B	5
23F	1
24F	1
9V	1
NT	1
<b>Total</b>	<b>23</b>

Table 3: Serotype distribution

Penicillin MIC	No
0.12	4
0.25	7
0.5	2
1	3
2	4
4	3
<b>Total</b>	<b>23</b>

Table 4: Penicillin MIC distribution

Strain No	Penicillin MIC	Ceftaroline Agardiffusion (1, 2, 3)			Ceftaroline MHK (1, 2, 3)		
		1	2	3	1	2	3
Strain 1	0.12	34	35		0,008	0,008	
Strain 2	0.12	34	34		0,015	0,008	
Strain 3	0.12	39	34	36	0,015	0,008	
Strain 4	0.12	34	34		0,015	0,015	
Strain 5	0.25	33	37	33	0,015	0,008	
Strain 6	0.25	48	36	34	0,015	0,015	
Strain 7	0.25	37	34	31	0,015	0,015	
Strain 8	0.25	34	35		0,015	0,015	
Strain 9	0.25	33	33		0,06	0,06	
Strain 10	0.25	39	36	36	0,015	0,008	
Strain 11	0.25	36	31	34	0,015	0,015	
Strain 12	0.5	36	37		0,12	0,12	
Strain 13	0.5	36	32	31	0,06	0,03	
Strain 14	1	30	31		0,03	0,06	
Strain 15	1	33	36	35	0,015	0,015	
Strain 16	1	34	33		0,12	0,06	
Strain 17	2	29	28		0,25	0,25	
Strain 18	2	35	31	28	0,12	0,06	
Strain 19	2	37	30	29	0,12	0,12	
Strain 20	2	42	38	39	0,25	0,06	0,25
Strain 21	4	36	30	28	0,25	0,25	
Strain 22	4	31	31		0,25	0,25	
Strain 23	4	41	33	34	0,12	0,12	

Table 7: MIC distribution (mg/L) and agardiffusion diameters (mm)

## Conclusions

- Penicillin non-susceptibility in *S. pneumoniae* is a rare event in Germany.
- In all cases examined ceftaroline would still be a treatment option since no resistant isolate could be identified.
- Zone diameters  $\geq$ 28 mm could be taken as an indication of susceptibility towards ceftaroline.