Comparative Activities of Ceftaroline and Ceftriaxone Against Bacterial Pathogens Associated with Community-Associated Respiratory Infections

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Abstract

Background: Ceftaroline fosamil is indicated for the treatment of community-associated (CA) pneumonia and ceftriaxone has an indication for lower respiratory tract infections (LRTI). This study provides a direct global comparison of the *in vitro* activity of these two key drugs against pathogens associated with respiratory tract infections. **Methods:** In all 15,187 isolates of *S. aureus*, *S. pneumoniae M. catarrhalis* and *H. influenzae* in 2012-2014 were collected globally from 39 countries in Asia-Pacific, Europe, Latin America and Middle East-Africa from CA respiratory tract specimens. The identification of all organisms was confirmed centrally by MALDI-TOF and broth microdilution susceptibility testing was done according to CLSI M100 and M7 guidelines. **Results**: Cumulative ceftaroline and ceftriaxone MIC distributions against target bacterial species are shown in the following table:

Organism	Drug	MIC (mg/L)/Cumulative %								
		≤0.06	0.12	0.25	0.5	1	2	4	8	16	≥32
MRSA (1,194)	Ceftaroline		0.2	7.0	47.8	**84.8**	**98.2**[a]	99.7	100		
	Ceftriaxone						0.4	0.8	1.5	9.0	**100**
		≤0.06	0.12	0.25	0.5	1	2	4	8	16	≥32
MSSA (1,036)	Ceftaroline	1.2	20.7	**85.2**	100						
	Ceftriaxone				0.3	0.9	14.5	**91.3**	97.5	99.8	100
		≤0.015	0.03	0.06	0.12	0.25	0.5	1	≥2		
S. pneumoniae (2,578)	Ceftaroline	71.4	77.5	83.7	**95.6**	99.2	100				
	Ceftriaxone	34.2	61.8	67.9	71.7	78.8	83.0	91.4	**100**		
		≤0.03	0.06	0.12	0.25	≤0.5	1	2			
M. catarrhalis (162)	Ceftaroline	33.3	62.3	**80.7**	96.3	100					
	Ceftriaxone				75.3[b]	**97.5**	100				
		≤0.03	0.06	0.12	0.25	≤0.5					
H. influenzae (368)	Ceftaroline	**98.4**	99.2	99.5	99.9	100					
	Ceftriaxone	**97.0**	98.9	99.5	99.7	100					

a. MIC_{50} values in bold and CLSI susceptibility percentages in dark grey where appropriate.
b. Lowest concentration tested

Based on MIC distributions ceftaroline was several fold more potent than ceftriaxone against MRSA, MSSA, *S. pneumoniae* and *M. catarrhalis*. Against MRSA and MSSA ceftaroline was 16-fold more active based upon MIC_{90} compared to ceftriaxone. Both drugs had comparable activity against *H. influenzae*. **Conclusions**: Based on these global MIC data ceftaroline exhibited potent *in vitro* activity against the major bacterial species associated with respiratory infections, in particular those that commonly cause community-associated infections. Ceftaroline also demonstrated an added advantage over ceftriaxone in being notably more active against *S. aureus*, including MRSA.

Introduction

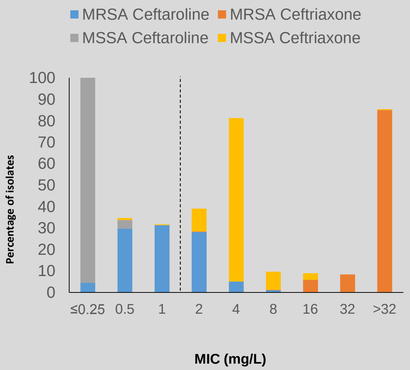
Ceftaroline fosamil is approved for the treatment of community-acquired (CA) pneumonia (excluding cases due to MRSA) and ceftriaxone has an indication for lower respiratory tract infections (LRTI). This study provides a direct global comparison of the *in vitro* activity of these two key drugs against pathogens associated with community-associated respiratory tract infections.

Materials & Methods

- In all 5,338 isolates of *S. aureus*, *S. pneumoniae M. catarrhalis* and *H. influenzae* in 2012-2014 were collected globally from 39 countries in Asia-Pacific, Europe, Latin America and Middle East/Africa from CA respiratory tract specimens.
- Organism identification was confirmed centrally using MALDI-TOF and antimicrobial susceptibility testing was performed by broth microdilution according to appropriate CLSI guidelines [1].

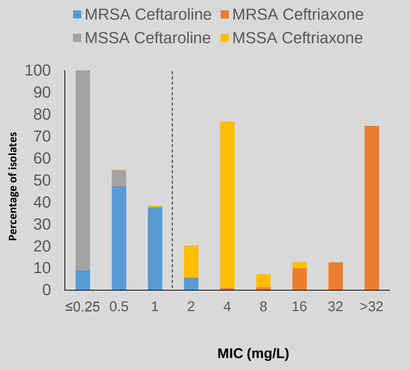
Results

Figure 1. MIC Distributions Among 535 *S. aureus* isolates from Asia-Pacific Countries.



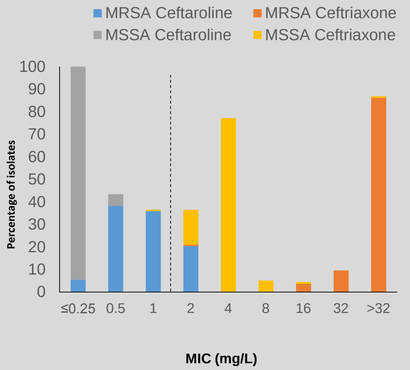
Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST and CLSI breakpoint criteria.

Figure 2. MIC Distributions Among 1187 *S. aureus* isolates from European Countries.



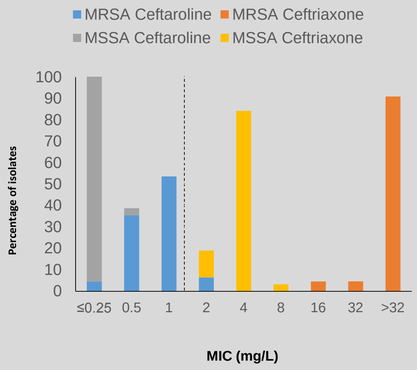
Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST and CLSI breakpoint criteria.

Figure 3. MIC Distributions Among 303 *S. aureus* isolates from Latin American Countries



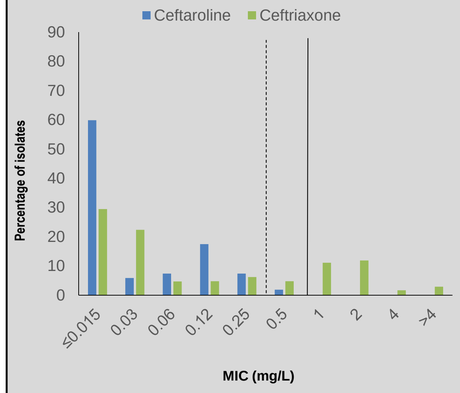
Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST and CLSI breakpoint criteria.

Figure 4. MIC Distributions Among 205 *S. aureus* isolates from Middle East-Africa



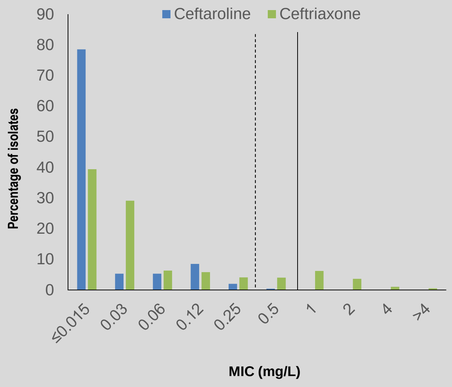
Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST and CLSI breakpoint criteria.

Figure 5. MIC Distributions Among 581 *S. pneumoniae* isolates from Asia-Pacific Countries.



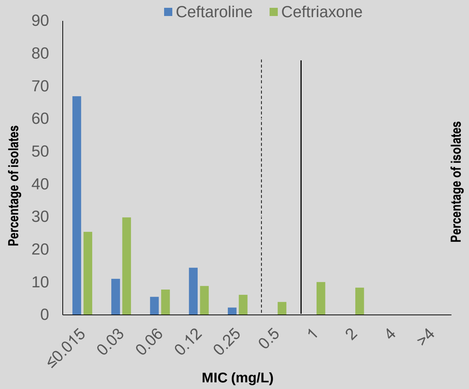
Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST breakpoint criteria. Solid line represents the susceptibility breakpoint for ceftriaxone consistent with EUCAST breakpoint criteria.

Figure 6. MIC Distributions Among 1608 *S. pneumoniae* isolates from European Countries.



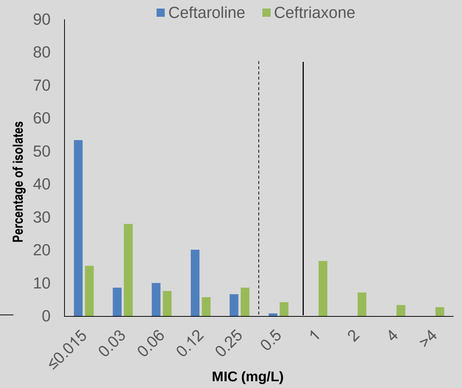
Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST breakpoint criteria. Solid line represents the susceptibility breakpoint for ceftriaxone consistent with EUCAST breakpoint criteria.

Figure 7. MIC Distributions Among 181 *S. pneumoniae* isolates from Latin American Countries



Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST breakpoint criteria. Solid line represents the susceptibility breakpoint for ceftriaxone consistent with EUCAST breakpoint criteria.

Figure 8. MIC Distributions Among 208 *S. pneumoniae* isolates from Middle East-Africa



Dashed line represents the susceptibility breakpoint for ceftaroline consistent with EUCAST breakpoint criteria. Solid line represents the susceptibility breakpoint for ceftriaxone consistent with EUCAST breakpoint criteria.

Results Summary

- All methicillin-susceptible *S. aureus* isolates (n=1036) were susceptible to ceftaroline with MIC_{90} value of 0.25 mg/L and 84.7% of the methicillin-resistant *S. aureus* (n=1194) were susceptible to ceftaroline with a MIC_{90} value of 2 mg/L.
- All *S. pneumoniae* isolates (n=2578) were susceptible to ceftaroline, regardless of susceptibility to penicillin with MIC_{90} values of 0.06 mg/L for penicillin-susceptible isolates and 0.5 mg/L for penicillin-resistant isolates. Only 32.1% and 11.4% of the penicillin-intermediate and –resistant *S. pneumoniae* isolates were susceptible to ceftriaxone, respectively.
- Regardless of β-lactamase production, both ceftaroline and ceftriaxone exhibited potent activity against all *H. influenzae* isolates (n= 368,100% susceptible) with MIC_{90} values of ≤0.015 mg/L and ≤0.03 mg/L for ceftaroline and 1 mg/L for ceftriaxone, respectively.
- The *M. catarrhalis* isolates (n=162) had MIC_{90} values of 0.12 mg/L for ceftaroline and 1 mg/L for ceftriaxone. Higher MIC values were observed among β-lactamase producing isolates.

Conclusions

- Based on these global MIC data ceftaroline exhibited potent *in vitro* activity against the major bacterial species associated with respiratory infections, in particular those that commonly cause community-associated infections.
- Ceftaroline was more potent than ceftriaxone against *S. aureus, S. pneumoniae* and *M. catarrhalis*.
- Ceftaroline demonstrated an added advantage over ceftriaxone in being notably more active against MRSA.

References and Acknowledgments:

1. Clinical Laboratory Standards Institute. 2015. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards - Tenth Edition. CLSI document M07-A10. Wayne, PA.
2. Clinical and Laboratory Standards Institute. 2016. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Sixth Informational Supplement. CLSI Document M100S. Wayne, PA.
3. The European Committee on Antimicrobial Susceptibility Testing – EUCAST Clinical Breakpoints 2015; http://www.eucast.org/clinical_breakpoints/

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