1673

In vitro Activities of Ceftaroline and Comparator Agents against Bacterial Pathogens Frequently Causing Community-Acquired Respiratory Tract Infections in Patients from a Global Population: ATLAS Surveillance Program 2017-2020

IHMA
2122 Palmer Drive
Schaumburg, IL 60173 USA
www.ihma.com

Meredith A. Hackel[1], Gregory G. Stone[2] , Daniel F. Sahm[1] [1]IHMA, Schaumburg IL, USA [2]Pfizer Inc., Groton, CT USA

Introduction

Community-acquired bacterial pneumonia (CABP) is a frequent cause of patient morbidity and mortality. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are frequent etiologic agents of CABP. Ceftaroline fosamil is a parenteral cephem approved for treatment of patients with CABP caused by *S. pneumoniae* (including cases with concurrent bacteremia), methicillin-susceptible *Staphylococcus aureus* (MSSA), *H. influenzae*, and some species of Enterobacterales. In this study we report the *in vitro* activity of ceftaroline and comparators against clinically relevant non-duplicate bacterial isolates from community-acquired respiratory tract infections (CARTI) pathogens by clinical laboratories in 54 countries as a part of the ATLAS (Antimicrobial Testing Leadership and Surveillance) global bacterial surveillance program.

Methods

Clinically relevant, non-duplicate, isolates cultured from respiratory specimens by clinical laboratories in 54 countries in 2017-2020 were collected by the ATLAS program. All isolates were sent to the central laboratory (IHMA, Schaumburg, IL, USA) where isolate identification was confirmed using MALDI-TOF mass spectrometry. In total, 2,284 isolates of *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, MSSA, and methicillin-resistant *S. aureus* (MRSA) were tested. The isolates (n/percent of total) originated from Asia/South Pacific (579/25.4%); Europe (1281/56.1%); Latin America (298/13.0%); Middle East/Africa (55/2.4%); and North America (Canada only) (71/3.1%). Antimicrobial susceptibility testing for ceftaroline and comparator agents was performed following CLSI M07 guidelines [1] for broth microdilution methodology. MICs were interpreted using 2022 CLSI M100 and 2015 M11 (*M. catarrhalis*) breakpoints [2, 3]. For staphylococci, the ceftaroline breakpoint for susceptible (≤1 µg/mL) is based on a dosage regimen of 600 mg administered every 12 h. The CLSI breakpoint for susceptible dose dependent (SDD) (≤4 µg/mL) is based on a dosage in adults of 800 mg every 8 h administered over 2 h.

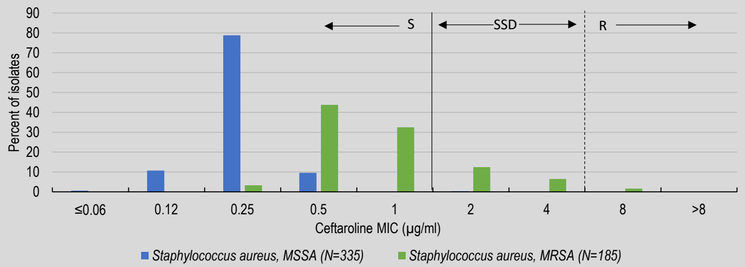
Results

Table 1. The *in vitro* activity of ceftaroline and comparator agents tested against isolates from community-acquired respiratory tract infections collected in 2017-2020

Bacterial Pathogen	Antimicrobial	Global			
		N	% S (S+SDD)	MIC_{90}	Range
Staphylococcus aureus, MRSA	Ceftaroline	185	79.5 (98.4)	2	0.25 - 8
	Amox/clav	108	0	>8	1 - >8
	Ceftriaxone	108	0	>64	1 - >64
	Erythromycin	185	26.0	>8	0.25 - >8
	Levofloxacin	211	29.4	>4	≤0.06 - >32
Staphylococcus aureus, MSSA	Ceftaroline	335	99.7	0.25	≤0.06 - 2
	Amox/clav	129	100	2	0.06 - >8
	Ceftriaxone	129	100	4	0.5 - >32
	Erythromycin	335	67.8	>4	≤0.12 - >8
	Levofloxacin	391	90.5	1	≤0.06 - 32
Streptococcus pneumoniae	Ceftaroline	635	99.4	0.12	≤0.004 - 8
	Amox/clav	424	90.3	2	≤0.015 - >8
	Ceftriaxone	826	93.8	1	≤0.015 - >4
	Erythromycin	825	67.4	>1	≤0.008 - >64
	Levofloxacin	826	98.4	1	≤0.06 - >8
S. pneumoniae, penicillin susceptible	Ceftaroline	412	100	0.015	≤0.004 - 0.12
	Amox/clav	263	100	0.03	≤0.015 - 0.12
	Ceftriaxone	537	100	0.06	≤0.015 - 1
	Erythromycin	536	81.7	>1	≤0.008 - >64
	Levofloxacin	537	99.6	1	≤0.06 - 8
S. pneumoniae, penicillin nonsusceptible	Ceftaroline	223	98.2	0.25	≤0.004 - 8
	Amox/clav	161	74.5	8	≤0.03 - >8
	Ceftriaxone	289	82.4	2	≤0.015 - >4
	Erythromycin	289	40.8	>1	≤0.015 - >64
	Levofloxacin	289	96.2	1	0.12 - >8
Haemophilus influenzae	Ceftaroline	414	99.3	0.06	≤0.015 - 1
	Amox/clav	700	98.4	2	≤0.12 - 16
	Ceftriaxone	700	99.9	≤0.06	≤0.03 - >4
	Levofloxacin	700	98.0	0.03	≤0.004 - >8
Moraxella catarrhalis	Ceftaroline	156	--	0.25	≤0.015 - 8
	Amox/clav	7	100	nc	≤0.12 - 0.25
	Ceftriaxone	7	100	nc	≤0.5 - 1
	Erythromycin	156	98.7	0.5	≤0.12 - >4
	Levofloxacin	156	100	0.06	≤0.015 - 2

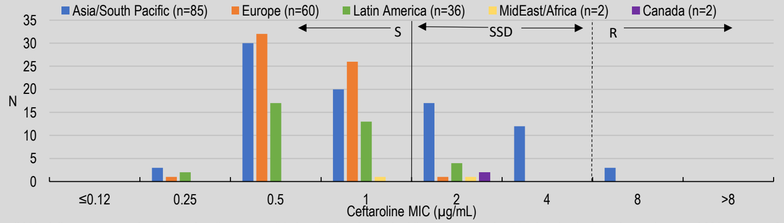
%S;% Susceptible; SDD, Susceptible-dose dependent based on a dosage of 600 mg every 8 hours; ; amox/clav, amoxicillin/clavulanate; %S for amoxicillin-clavulanate and ceftriaxone determined by oxacillin susceptibility; nc, not calculated when N≤10; --, no ceftaroline breakpoints available for *Moraxella catarrhalis*

Figure 1. Ceftaroline MIC distribution for MRSA and MSSA isolates from community acquired respiratory tract infections, 2017-2020



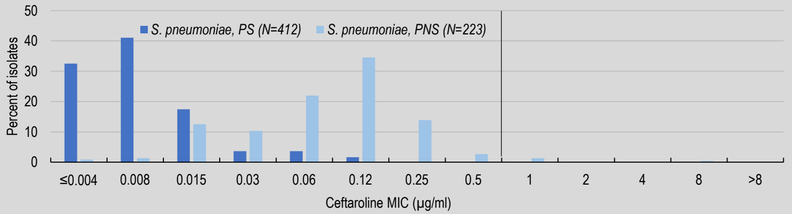
The solid black line represents the CLSI ceftaroline susceptible breakpoint; the dashed line represents the SDD breakpoint based on a dosage of 600 mg every 8 hours administered over 2 hours; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; S, susceptible; SDD, susceptible dose-dependent; R, resistant

Figure 2. Ceftaroline MIC distribution for methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from community acquired respiratory tract infections by region, 2017-2020



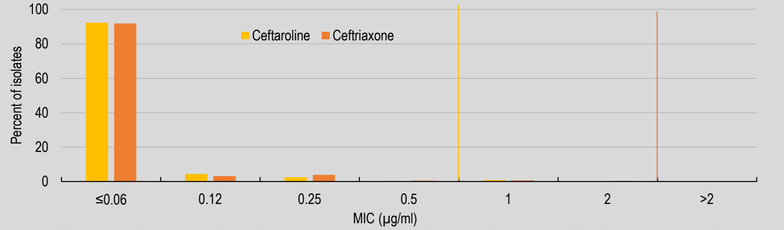
The solid black line represents the CLSI ceftaroline susceptible breakpoint; the dashed line represents the SDD breakpoint based on a dosage of 600 mg every 8 hours administered over 2 hours; SDD, susceptible dose-dependent; R, resistant

Figure 3. Ceftaroline MIC distribution for *Streptococcus pneumoniae* (PS-penicillin susceptible and PNS-penicillin non-susceptible) isolates from community acquired respiratory tract infections, 2017-2020



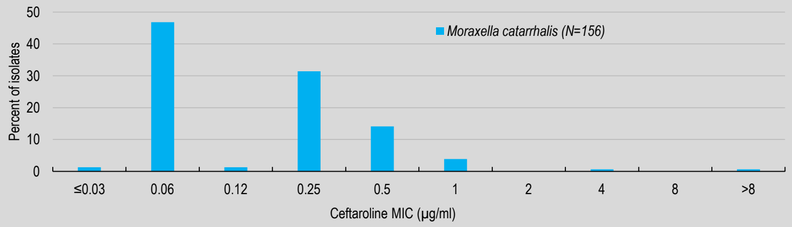
The solid line indicates the CLSI susceptible MIC breakpoint for ceftaroline

Figure 4. Ceftaroline and ceftriaxone MIC distributions for *Haemophilus influenzae* from community acquired respiratory tract infections, 2017-2020



The yellow line indicates the CLSI susceptible MIC breakpoint for ceftaroline; the orange line indicates the CLSI susceptible MIC breakpoint for ceftriaxone

Figure 5. Ceftaroline MIC distributions for *Moraxella catarrhalis* isolates from community acquired respiratory tract infections, 2017-2020



Results

- >99% of MSSA were susceptible to ceftaroline based on a dosage of 600 mg every 12h (Table 1, Figure 1).
- 79.5% of MRSA were susceptible to ceftaroline. (Table 1, Figure 1). Percent susceptible for comparator agents was 29.4% for levofloxacin and 26.0% for erythromycin (Table 1).
- Thirty-five (18.9%) MRSA were ceftaroline-susceptible-dose-dependent (SDD, MIC 2-4 µg/mL) based on a dosage of 600 mg every 8h administered over 2h, with the majority from (n/total from country) China (18/31) and S. Korea (8/24). Three isolates, all from China, were resistant to ceftaroline (MIC of 8 µg/mL) (Figure 2).
- 99.4% of *S. pneumoniae* were susceptible to ceftaroline, including 100% of penicillin-susceptible isolates and 98.2% of penicillin-nonsusceptible isolates (Table 1, Figure 3).
- 99.3% of *H. influenzae* were susceptible to ceftaroline.
- There are no established breakpoints for ceftaroline against *M. catarrhalis*. The ceftaroline MIC_{90} was 0.25 µg/mL.

Conclusions

Ceftaroline demonstrated potent *in vitro* activity against current pathogens associated with community-acquired respiratory tract infections from a global collection.

References

1. Clinical and Laboratory Standards Institute (CLSI) 2018. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standards-Eleventh Edition*. CLSI Document M07-A11 (ISBN 1-56238-836-3). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
2. Clinical and Laboratory Standards Institute (CLSI), 2022. *Performance Standards for Antimicrobial Susceptibility Testing. 32nd Ed.* CLSI Supplement M100 (ISBN 978-1-68440-134-5). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
3. Clinical and Laboratory Standards Institute. 2015. *Methods for Antimicrobial Dilution and Disk Susceptibility Testing of Infrequently Isolated or Fastidious Bacteria;* CLSI Document M45-A3 (ISBN 1-56238-917-3). CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.

Disclosures

This study was sponsored by AstraZeneca (AZ). AZ's rights to ceftaroline fosamil were acquired by Pfizer in December 2016. MH and DS are employees of IHMA, who received fees from Pfizer for the conduct of the study and were paid consultants to Pfizer in connection with the development of this abstract/poster. GS, an employee of and shareholder in AZ at the time of the study, is currently an employee of Pfizer.

Presented at IDWeek 2022, October 19-23, 2022 in Washington, D.C.