

Meredith A. Hackel¹, Gregory G. Stone², Daniel F. Sahn¹ ¹IHMA, Schaumburg IL, USA ²Pfizer 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 $\mu\text{g/mL}$) is based on a dosage regimen of 600 mg administered every 12 h. The CLSI breakpoint for susceptible dose dependent (SDD) (≤ 4 $\mu\text{g/mL}$) is based on a dosage in adults of 800 mg every 8 h administered over 2 h.

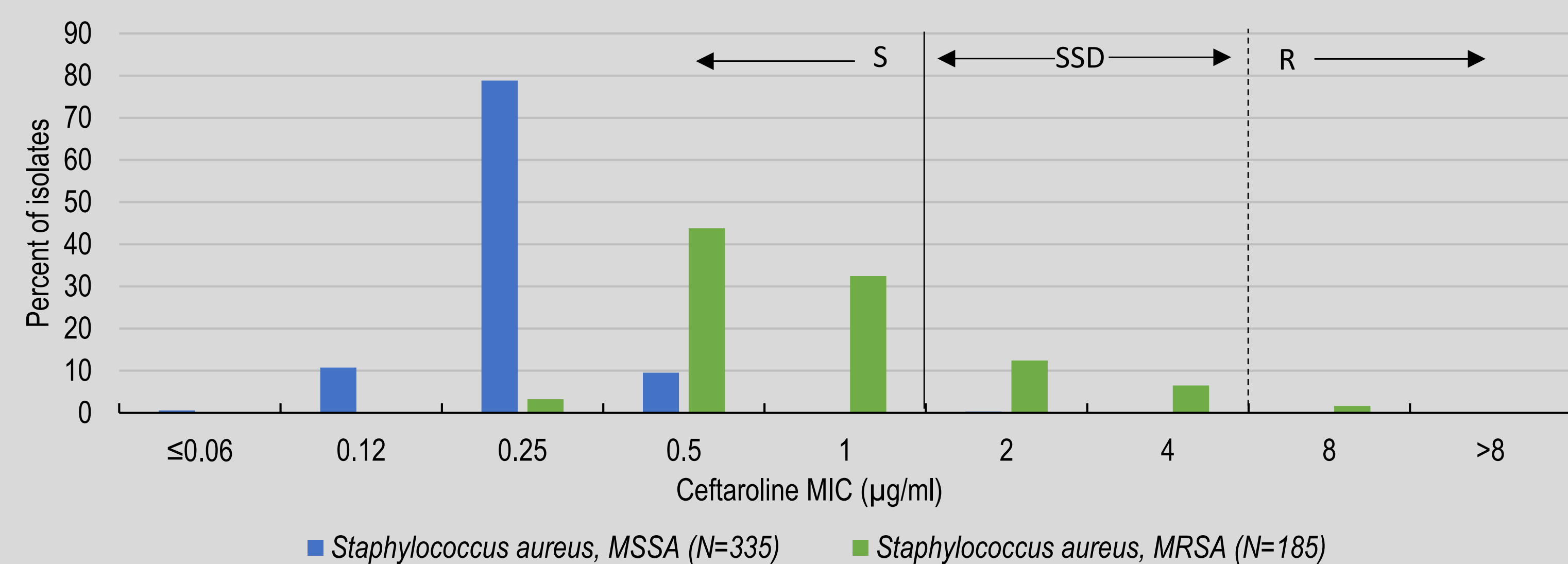
Results

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 |
| <i>Staphylococcus aureus</i> , 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 |
| | <i>Staphylococcus aureus</i> , MSSA | Ceftaroline | 335 | 99.7 | 0.25 |
| 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 |
| <i>Streptococcus pneumoniae</i> | | Ceftaroline | 635 | 99.4 | 0.12 |
| | 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 |
| | <i>S. pneumoniae</i> , penicillin susceptible | Ceftaroline | 412 | 100 | 0.015 |
| 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 |
| <i>S. pneumoniae</i> , penicillin nonsusceptible | | Ceftaroline | 223 | 98.2 | 0.25 |
| | 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 |
| | <i>Haemophilus influenzae</i> | Ceftaroline | 414 | 99.3 | 0.06 |
| 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 |
| <i>Moraxella catarrhalis</i> | 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 |

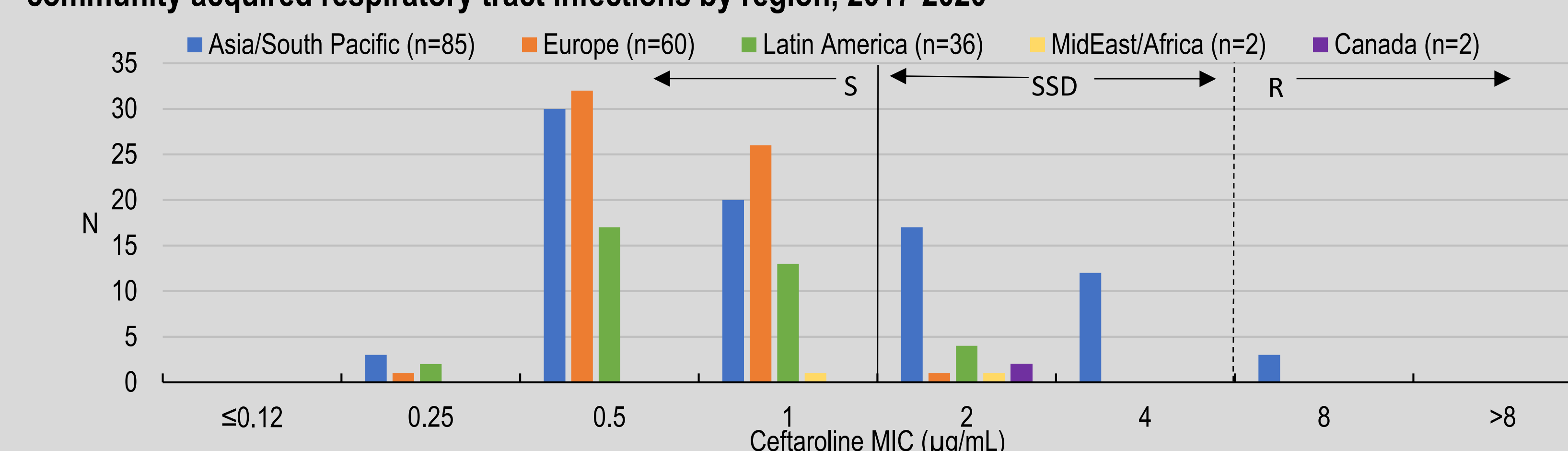
%S: % Susceptible; SDD, Susceptible-dose dependent based on a dosage of 600 mg every 8 hours; amox/clav, amoxicillin/clavulanate; %S for amoxicillin-clavulanate and ceftriaxone determined by oxacillin susceptibility; nc, not calculated when N \leq 10; --, no ceftaroline breakpoints available for *Moraxella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

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



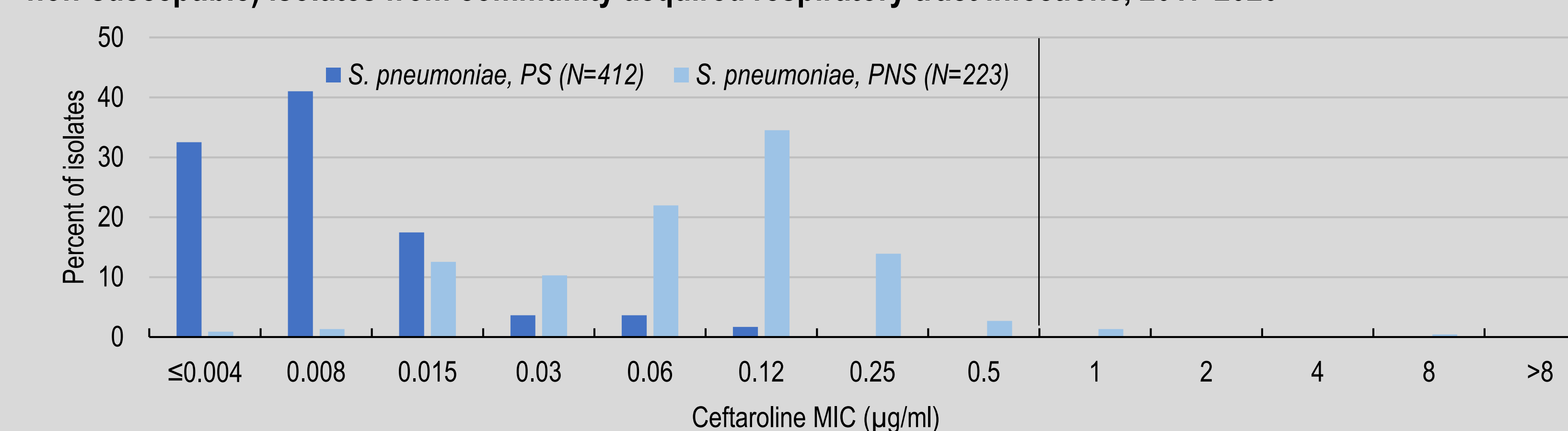
The solid black line represents the CLSI ceftaroline susceptible breakpoint; the dashed line represents the SDD breakpoint based on a dosage of 600 mg every 8 hours administered over 2 hours; MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*; S, susceptible; SDD, susceptible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



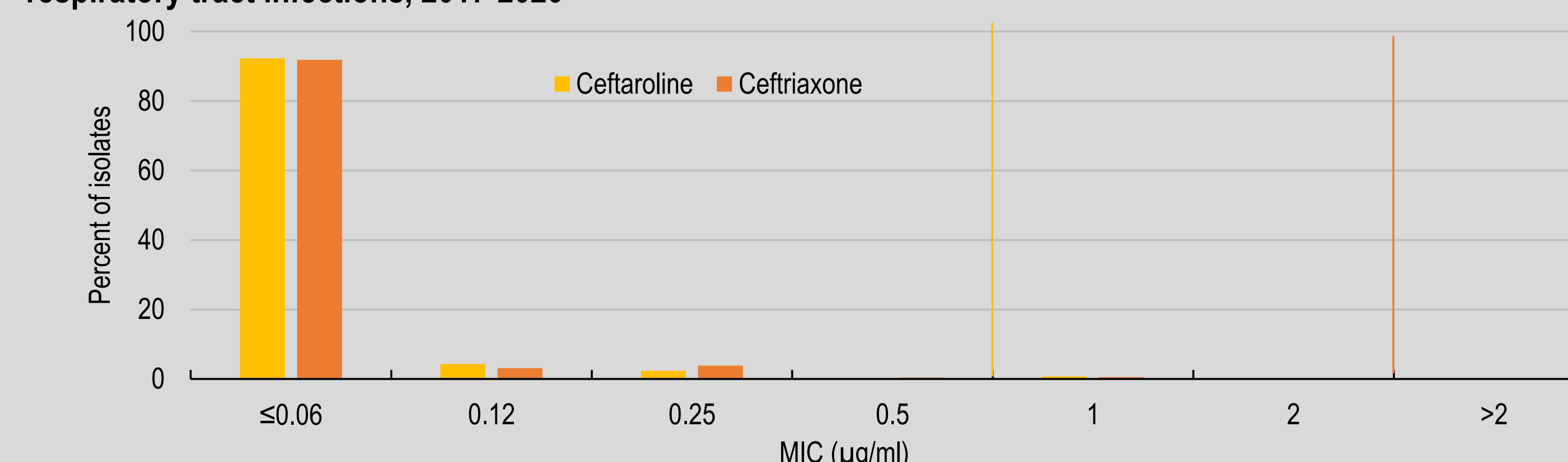
The solid black line represents the CLSI ceftaroline susceptible breakpoint; the dashed line represents the SDD breakpoint based on a dosage of 600 mg every 8 hours administered over 2 hours; SDD, susceptible dose-dependent; R, resistant

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



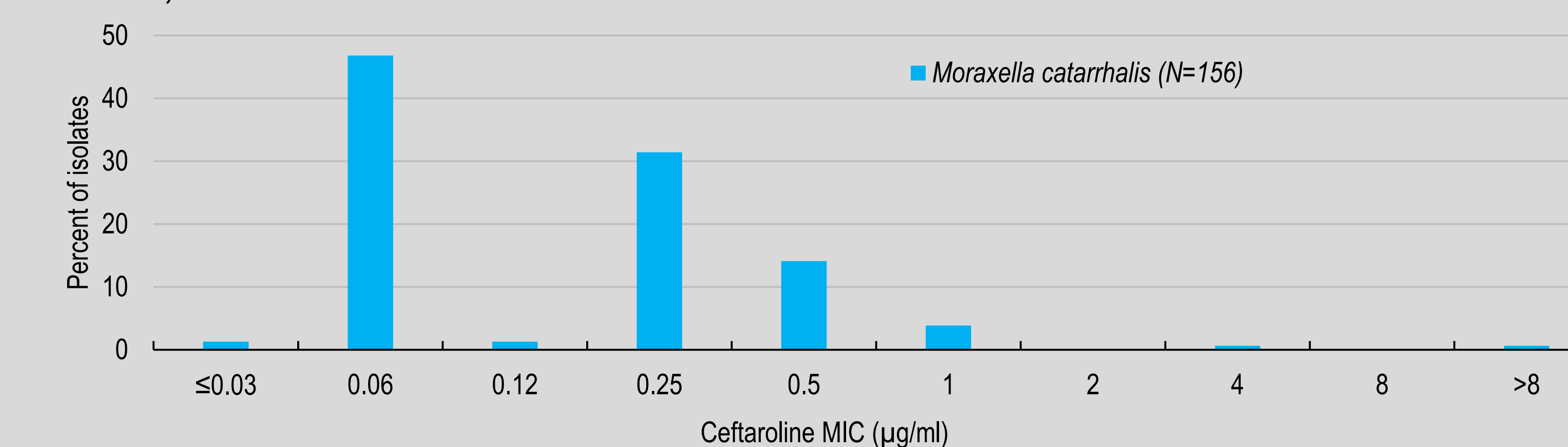
The solid line indicates the CLSI susceptible MIC breakpoint for ceftaroline

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 $\mu\text{g/mL}$) 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 $\mu\text{g/mL}$) (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 MIC₉₀ was 0.25 $\mu\text{g/mL}$.

Conclusions

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

References

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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.