The emergence of clinically important antimicrobial resistance continues to escalate, involving greater numbers of pathogens, clinical settings, and geographic areas. This worldwide threat has resulted in higher rates of morbidity and mortality. Despite this, comprehensive audits of available/candidate new antimicrobial agents have identified only a limited number of new or novel compounds to address these problems [1, 2]. The Infectious Diseases Society of America has launched the “10 × 20” initiative, which calls for 10 new antibiotics by 2020 [3]. To solve this problem of drug resistance and achieve the “10 × 20” goal, it is mandatory that numerous stakeholders collaborate to make discovery of antimicrobials a priority for the pharmaceutical industry, national/regional governments, practicing physicians and societies, as well as the public [3]. Fortunately, one of the initial agents addressing antimicrobial resistance, ceftaroline fosamil [4, 5], has been approved by regulatory agencies in North America (the US Food and Drug Administration) and Europe (the European Medicines Agency). Comprehensive review of current anti-infective research indicates that several new antibacterial compounds are in the pipeline [6].

Currently available clinical trials data and information on in vitro activity for ceftaroline is fragmented or focuses on microbiologic activity for strains isolated during or before 2009 [7–10]. In this supplement, authors summarize all available clinical trials leading to ceftaroline approvals for acute bacterial skin and skin structure infections (ABSSSIs) and community-acquired bacterial pneumonia (CABP). In addition, authors provide a detailed analysis of the AWARE Ceftaroline Surveillance Program through 2010 in the United States.

File, Wilcox, and Stein [11] summarize the results of 4 phase 3 noninferiority design clinical trials (for CABP, FOCUS 1 and 2; for ABSSSI, CANVAS 1 and 2) that showed ceftaroline to be comparable to the other therapeutic agents (ceftriaxone and vancomycin plus aztreonam). The authors also emphasize subset analysis results, such as markedly higher cure rates in patients receiving ceftaroline in the Streptococcus pneumonia subgroup. Of similar importance, the safety profile of ceftaroline was reviewed and considered to be acceptable and most like that of other cephalosporins.

The in vitro ceftaroline resistance surveillance results (presented here) up to and including 2010 [12–15] concentrate on various pathogen subgroups for which this new cephalosporin would be clinically applied. Sader and colleagues [12] demonstrate that patient age had little influence on ceftaroline MIC results when testing staphylococcal isolates, including those obtained from younger patients (age, ≤17 years), thus opening the door for trials in this oft-neglected pediatric subgroup [12]. Even in elderly patients (age, >50 years), the most elevated percentage of Staphylococcus aureus isolates that were ceftaroline nonsusceptible was only 1.2%. Similarly, ceftaroline nonsusceptibility among respiratory pathogens from 2008–2010 was unusual (1.3% of S. pneumoniae isolates), and the ceftaroline potency was 16-fold greater than that of ceftiraxone [13].

Geographic influence on ceftaroline minimum inhibitory concentrations (MICs) for methicillin-resistant S. aureus (MRSA) was also minimal (96.7%–100.0% of isolates were susceptible) across all 9 US Census regions [14]. Moreover, ceftaroline inhibited all MRSA at ≤2
µg/mL, a value one-doubling dilution step above the US FDA break point. Only Enterobacteriaceae susceptibility was significantly different between geographic regions, driven by the prevalence of various types of β-lactamases and carbapenemases. Finally, Farrell et al outline the ceftaroline potencies against the very challenging subsets of multidrug-resistant S. aureus and pneumococci, using a 3-year (2008–2011) collection of AWARE study isolates [15]. A total of 30.1% of S. pneumoniae isolates were multidrug resistant, but only 4.4% were ceftaroline nonsusceptible, in contrast to 10.9% for ceftriaxone. Similarly, MRSA isolates had a ceftaroline MIC90 of 1 µg/mL, regardless of multidrug-resistant status [15]. A total of 30.1% of S. pneumoniae isolates were multidrug resistant, but only 4.4% were ceftaroline nonsusceptible, in contrast to 10.9% for ceftriaxone. Similarly, MRSA isolates had a ceftaroline MIC90 of 1 µg/mL, regardless of multidrug resistance pattern (95.8%–99.4% of isolates were susceptible). We hope the clinical and in vitro microbiology surveillance data provided in this supplement enable physicians and clinical microbiologist to use ceftaroline in contemporary practice appropriately, as outlined in the product package insert [16].

Notes

Supplement sponsorship. This article was published as part of a supplement entitled “Ceftaroline Applications for Therapy in the United States,” sponsored by Forest Laboratories, Inc (New York, NY).

Potential conflicts of interest. G. R. C. has received honorarium from Forest. R. N. J. has received institutional support through Forest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

11. Sader HS, Flamm RK, Farrell DJ, Jones RN. Activity results of staphylococcal isolates from pediatric, adult and elderly patients; AWARE ceftaroline surveillance program (USA, 2010). In this supplement.