P1339
Paper Poster Session
New agents in clinical development against gram-positive bacteria

Delafloxacin activity tested against bacterial pathogens from 44 medical centres in Europe and Israel (2014)

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Background: Delafloxacin is an anionic investigational fluoroquinolone antibiotic currently in phase III development in the United States for the treatment of acute bacterial skin and skin structure infections. It is active against Gram-positive and -negative bacteria including anaerobes and atypical bacteria. Included in its activity spectrum are fluoroquinolone- and methicillin-resistant staphylococci. The aim of this study was to examine the susceptibility profiles of delafloxacin when tested against contemporary clinical isolates collected from medical centres in Europe and Israel during 2014.

Material/methods: A total of 2,075 Gram-positive and -negative, non-duplicate, non-consecutive, bacterial clinical isolates collected from patients in 44 medical centres across >20 European countries and Israel were selected. Isolate identity was confirmed at a central monitoring laboratory using standard bacteriologic algorithms and the use of MALDI-TOF when necessary. Antibacterial susceptibility testing was performed by broth microdilution per CLSI guidelines. EUCAST breakpoints were used to determine susceptibility rates.

Results: The delafloxacin $MIC_{50/90}$ for all *S. aureus* was ≤0.004/0.12 mg/L. Delafloxacin was the most potent ($MIC_{50/90}$, ≤0.004/≤0.004 mg/L) antimicrobial tested against MSSA and based on MIC_{90} was at least 64-fold more potent than ceftaroline and levofloxacin. Delafloxacin ($MIC_{50/90}$, 0.12/0.25 mg/L) tigecycline ($MIC_{50/90}$, 0.06/0.12 mg/L), daptomycin ($MIC_{50/90}$, 0.25/0.5 mg/L), and trimethoprim-sulfamethoxazole ($MIC_{50/90}$, ≤0.5/≤0.5 mg/L) were the most potent antimicrobials tested against MRSA; susceptibility to vancomycin ($MIC_{50/90}$, 1/1 mg/L) and linezolid ($MIC_{50/90}$, 0.5/1 mg/L) was 100.0%. There were high levels of resistance against levofloxacin (73.4% resistant) and erythromycin (64.1%). Delafloxacin ($MIC_{50/90}$, 0.06/1 mg/L) and linezolid ($MIC_{50/90}$, 1/1 mg/L) were the most active antimicrobials tested against *Enterococcus faecalis*. Against *Streptococcus pneumoniae*, delafloxacin was the most active agent ($MIC_{50/90}$, 0.008/0.015 mg/L; highest MIC, 0.03 mg/L). Delafloxacin was eight-fold more active than ceftaroline ($MIC_{50/90}$, ≤0.015/0.12 mg/L; 98.7% susceptible); 16-fold more active than moxifloxacin ($MIC_{50/90}$, ≤0.12/0.25 mg/L; 100.0% susceptible), and 64-fold more active than levofloxacin ($MIC_{50/90}$, 1/1 mg/L; 100.0% susceptible). Delafloxacin was active against β-haemolytic streptococci (MIC_{90}, 0.015 mg/L). Overall, against 750 Enterobacteriaceae, the delafloxacin $MIC_{50/90}$ was 0.06/4 mg/L with 78.3% of isolates inhibited at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibilities were 77.1 and 80.9%, respectively and ceftazidime susceptiblity was 77.2%. Delafloxacin inhibited 73.0% of *Pseudomonas aeruginosa* at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibility rates were 66.0 and 62.0%, respectively. Colistin was the only agent which exhibited at least 90% susceptibility. Delafloxacin inhibited 29.0% of *Acinetobacter baumannii* at ≤1 mg/L. Ciprofloxacin and levofloxacin susceptibilities were poor (17.0%). Colistin (90.0% susceptible) was the only agent to achieve susceptibility >90%.

Conclusions: Delafloxacin provides a number of *in vitro* advantages in potency and spectrum when directly compared to currently marketed fluoroquinolones, especially with its enhanced activity against

S. aureus including MRSA strains, and its improved potency against *S. pneumoniae,* β-hemolytic streptococci, and *E. faecalis.* Further evaluation in clinical trials appears warranted.

		MIC in mg/L:	
Select organisms	**n**	**Delafloxacin**	**Levofloxacin (%S)**
S. aureus	250	0.12	>4 (77.6%)
MRSA	64	0.25	>4 (26.6%)
E. faecalis	150	1	>4 (-)
S. pneumoniae	150	0.015	1 (100.0%)
S. agalactiae	75	0.015	1 (97.3%)
S. pyogenes	150	0.015	1 (96.0%)
Enterobacteriaceae	750	4	>4 (80.9%)
P. aeruginosa.	100	>4	>4 (62.0%)
A. baumannii	100	>4	>4 (17.0%)