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Activity of the Fluoroquinolone JNJ-Q2 Tested Against Contemporary (2012) Pathogens Isolated from the Global SENTRY Surveillance Platform

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ABSTRACT

Background: JNJ-Q2 exhibits potent bactericidal activity against Gram-positive (GP) and some Gram-negative (GN) pathogens, including methicillin-resistant (MR) *S. aureus* (SA), and *S. pneumoniae* (SPN) including penicillin-resistant (PEN-R) strains.

Methods: Non-duplicate, prospectively collected isolates from the SENTRY platform were recovered from patients with infections including community-acquired and nosocomial respiratory tract, wound or skin and skin structure, and bloodstream infections. Isolate identity was confirmed by JMI Laboratories (North Liberty, Iowa, USA) and reference susceptibility was performed using validated panels (CLSI M07-A9 [2012]). Interpretive criteria were as published (CLSI M100-S23 [2013] and EUCAST [2013]).

Results: JNJ-Q2 was highly active against SPN, *H. influenzae* (HI), and *M. catarrhalis* (MC). All 2,162 SPN isolates were inhibited at ≤0.25 µg/mL (MIC_{90}, 0.015 µg/mL). 17.5/1.3% of isolates were PEN-R (MIC, ≥2 µg/mL/ MIC, ≥8 µg/mL), 36.7% erythromycin (ERY)-R, 26.6% tetracycline (TET)-R and 1.2% levofloxacin (LEV)-R. The MIC_{90} values for HI and MC were 0.015 µg/mL. The $MIC_{50/90}$ for JNJ-Q2 against 4,537 *S. aureus* (37.3% MRSA) was 0.008/0.25 µg/mL. LEV-R, ERY-R, and clindamycin-R were at 31.5, 43.0 and 16.4 respectively. The activity of JNJ-Q2 was lower in LEV-R strains; LEV-R MRSA and LEV-R methicillin-susceptible (MS) SA ($MIC_{50/90}$, 0.25/0.5 and 0.12/0.25 µg/mL, respectively) compared to LEV-susceptible (S) strains ($MIC_{50/90}$, 0.008/0.015 µg/mL). The JNJ-Q2 $MIC_{50/90}$ for Enterobacteriaceae (ENT) was ($MIC_{50/90}$, 0.12/2 µg/mL) and for *P. aeruginosa* (PSA; $MIC_{50/90}$, 1/>4 µg/mL). JNJ-Q2 was 2-4X more potent than moxifloxacin (MOX) and 4X less potent than ciprofloxacin (CIP) against ENT and PSA (MIC_{50} values). Greater activity against R ENT strains was noted by the MIC_{90} (>2X lower). JNJ-Q2 ($MIC_{50/90}$, 1/2 µg/mL) was more potent than LEV, MOX, and CIP ($MIC_{50/90}$, >4/>4 µg/mL) against *Acinetobacter* spp. (ASP). Colistin (COL) and tigecycline (TIG) were the only other agents showing potent activity against ASP ($MIC_{50/90}$, 1/2 µg/mL).

Conclusions: JNJ-Q2 exhibited a broad-spectrum of activity against GP and some GN pathogens including multi-drug-resistant (MDR) strains of SA and SPN. Its activity against MDR ASP was equal to COL and TIG and may merit further evaluation.

INTRODUCTION

JNJ-Q2 is a novel fluorinated 4-quinolone with potent activity against Gram-positive (including MRSA) and some Gram-negative pathogens, and has been shown to have balanced potency against both DNA gyrase and topoisomerase IV. JNJ-Q2 is in clinical development for the treatment of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI).

The objectives of this study were to determine comparative *in vitro* activity of JNJ-Q2 tested against clinical isolates collected in 2012 relevant to CABP and ABSSSI, and to monitor the activity of JNJ-Q2 compared to numerous other broad-spectrum antimicrobial agents when tested against contemporary clinical isolates in North American, European, Asia-Western Pacific and Latin American medical centers for the year 2012.

MATERIALS AND METHODS

Bacterial isolates. A total of 16,176 isolates were obtained in the 2012 surveillance program. Distribution by geographical region (number of isolates) were as follows: Asia West-Pacific (2,137), Europe (6,037), Latin America (1,591) and North America (6,411). Non-duplicate, prospectively collected bacterial isolates from the SENTRY Antimicrobial Surveillance Program were recovered consecutively from patients with bloodstream infections, community-acquired and nosocomial respiratory tract infections, and wound or skin and skin structure infections. Isolates were identified by the submitting laboratories and confirmed by JMI Laboratories (North Liberty, Iowa, USA) using standard bacteriologic algorithms and methodologies, including the use of the Vitek® 2 Identification System (bioMerieux, Hazelwood, Missouri, USA) and MALDI-TOF (Bruker, Germany) when appropriate.

Susceptibility testing. Reference dry-form broth microdilution method (CLSI M07-A9 [2012]) was applied using validated trays produced by ThermoFisher Scientific (Cleveland, Ohio, USA), applying cation-adjusted Mueller-Hinton broth with supplements for fastidious species. Haemophilus Test Medium (HTM) and 2-5% lysed horse blood were used for *Haemophilus* spp. and streptococcal testing, respectively. Interpretive criteria for the comparator agents were as published by the CLSI M100-S23 (2013) and EUCAST (2013). CLSI quality control (QC) MIC ranges were utilized to assure accurate test performances (CLSI, 2013). QC was tested daily with *Haemophilus influenzae* ATCC 49247, *Staphylococcus aureus* ATCC 29213, *Streptococcus pneumoniae* ATCC 49619, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. All QC results were within established ranges.

RESULTS

- Activity of JNJ-Q2 against *S. pneumoniae.*
  - JNJ-Q2 was very active ($MIC_{50/90}$, 0.015/0.015 µg/mL) against all 2,162 pneumococci with all isolates being inhibited at MIC values of ≤0.25 µg/mL (**Table 1**).
  - JNJ-Q2 was the most active antimicrobial agent tested against *S. pneumoniae*, including strains resistant to the other tested fluoroquinolones (**Table 2**). The JNJ-Q2 MIC_{90} value (0.015 µg/mL) was 128-fold lower than ciprofloxacin (2 µg/mL), 64-fold lower than levofloxacin (1 µg/mL) and 16-fold lower than moxifloxacin (0.25 µg/mL).
  - Resistance to oral penicillin V was 17.5% and non-susceptibility to ceftriaxone was 9.9% (CLSI criteria). Erythromycin, tetracycline, and trimethoprim/sulfamethoxazole resistance rates were all high overall (36.7, 26.6, and 21.4%, respectively). The highest susceptibility rates were for vancomycin (100.0%) and linezolid (100.0%; **Table 2**).
- Activity of JNJ-Q2 against *H. influenzae* and *M. catarrhalis.*
  - JNJ-Q2 was very active against 1,295 *H. influenzae* isolates ($MIC_{50/90}$, 0.008/0.015 µg/mL) with 100.0% isolates being inhibited at a MIC of ≤1 µg/mL (**Table 1**). The $MIC_{50/90}$ values did not differ among β-lactamase-positive and -negative strains ($MIC_{50/90}$, 0.008/0.015 µg/mL; data not shown). Levofloxacin, moxifloxacin and ciprofloxacin also demonstrated excellent activity against most isolates (>99.5% susceptibility by both CLSI and EUCAST interpretations).
  - JNJ-Q2 demonstrated excellent activity against all 505 *M. catarrhalis* isolates ($MIC_{50/90}$, 0.015/0.015 µg/mL; **Table 1**) with inhibition of all isolates observed at a MIC of ≤0.06 µg/mL. Levofloxacin, moxifloxacin and ciprofloxacin also demonstrated excellent activity against *M. catarrhalis* (**Table 2**).
- Activity of JNJ-Q2 against *S. aureus.*
  - JNJ-Q2 demonstrated good activity overall ($MIC_{50/90}$, 0.008/0.25 µg/mL) against 4,537 *S. aureus* (SA) with 99.7% all isolates inhibited at a MIC of ≤1 µg/mL (**Table 1**). There were 12 isolates (0.3% of 4,537) at 2 µg/mL and no isolates at >2 µg/mL. All 12 isolates were oxacillin- (methicillin-) resistant (MR), and were levofloxacin-, moxifloxacin-, and ciprofloxacin- resistant (MIC, >4 µg/mL). JNJ-Q2 (MIC_{90}, 0.25 µg/mL) was 16-fold more potent than moxifloxacin (MIC_{90}, 4 µg/mL) and at least 16-fold more potent than ciprofloxacin and levofloxacin (MIC_{90}, both >4 µg/mL; **Table 2**).
  - Overall resistance rates were high for oxacillin (MRSA, 37.3%), erythromycin (43.0%), and clindamycin (16.4%). No resistance was observed when *S. aureus* were tested against tigecycline and susceptibilities to daptomycin, linezolid, and vancomycin were >99.9% (**Table 2**).
- Activity of JNJ-Q2 against β-hemolytic streptococci (βHS) and viridans group streptococci (VGS).
  - JNJ-Q2 demonstrated excellent *in vitro* activity ($MIC_{50/90}$, 0.015/0.015 µg/mL) against βHS (including 535 *S. pyogenes*) inhibiting all isolates at a MIC value of ≤0.25 µg/mL (**Table 1**). JNJ-Q2 (MIC_{90}, 0.015 µg/mL) demonstrated a 16-fold greater potency than moxifloxacin (MIC_{90}, 0.25 µg/mL), 64-fold greater potency than levofloxacin (MIC_{90}, 1 µg/mL), and 64-fold greater potency than ciprofloxacin (MIC_{90}, 1 µg/mL; **Table 2**).
  - JNJ-Q2 also demonstrated excellent *in vitro* activity ($MIC_{50/90}$, 0.015/0.015 µg/mL) against 606 isolates of VGS inhibiting all isolates at a MIC value of ≤0.5 µg/mL (**Table 1**). JNJ-Q2 (MIC_{90}, 0.015 µg/mL) demonstrated a 16-fold greater potency than moxifloxacin (MIC_{90}, 0.25 µg/mL), 128-fold greater potency than levofloxacin (MIC_{90}, 2 µg/mL), and 256-fold greater potency than ciprofloxacin (MIC_{90}, 4 µg/mL; **Table 2**).
- Activity of JNJ-Q2 against enterococci.
  - JNJ-Q2 showed good *in vitro* activity ($MIC_{50/90}$, 0.25/2 µg/mL) against 853 isolates of *Enterococcus* spp. (*E. faecalis* 548 isolates, *E. faecium* 305 isolates) inhibiting 79.1% isolates at ≤1 µg/mL and 99.9% of isolates at a MIC value of ≤4 µg/mL (**Table 1**). Ampicillin and vancomycin resistance were 32.7 and 18.6%, respectively (**Table 2**). JNJ-Q2 was more active against vancomycin susceptible ($MIC_{50/90}$, 0.06/1 µg/mL) than vancomycin non-susceptible ($MIC_{50/90}$, 2/4 µg/mL; **Table 1**) strains.
- Activity of JNJ-Q2 against Enterobacteriaceae.
  - Ciprofloxacin resistance was 23.2% overall against 3,543 Enterobacteriaceae (**Table 2**). JNJ-Q2 showed good *in vitro* activity ($MIC_{50/90}$, 0.12/2 µg/mL) and based on the MIC_{90} values demonstrated at least four-fold greater potency than moxifloxacin ($MIC_{50/90}$, ≤0.12/>4 µg/mL).
  - JNJ-Q2 demonstrated similar activities against *E. coli* ($MIC_{50/90}$, 0.03/2 µg/mL), *Klebsiella* spp. ($MIC_{50/90}$, 0.06/4 µg/mL), *Proteus mirabilis* ($MIC_{50/90}$, 0.12/4 µg/mL), *Citrobacter* spp. ($MIC_{50/90}$, 0.06/2 µg/mL), *Enterobacter* spp. ($MIC_{50/90}$, 0.06/2 µg/mL), indole-positive *Proteus* spp. ($MIC_{50/90}$, 0.12/4 µg/mL), and *Serratia* spp. ($MIC_{50/90}$, 0.5/1 µg/mL; **Table 1**). JNJ-Q2 was less active against ESBL-phenotypes of Enterobacteriaceae ($MIC_{50/90}$, 2/>4 µg/mL) than non-ESBL-phenotypes ($MIC_{50/90}$, 0.06/0.5 µg/mL; **Table 1**) which was directly related to the prevalence of ciprofloxacin resistance in the subpopulation (non-ESBL vs. ESBL).
- Activity of JNJ-Q2 against *P. aeruginosa*, *Acinetobacter* spp., and *Stenotrophomonas maltophilia.*
  - Based on MIC_{50} values, JNJ-Q2 ($MIC_{50/90}$, 1/>4 µg/mL) demonstrated two-fold better activity than moxifloxacin ($MIC_{50/90}$, 2/>4 µg/mL), two-fold less activity compared to levofloxacin ($MIC_{50/90}$, 0.5/>4 µg/mL), and four-fold lower activity than ciprofloxacin ($MIC_{50/90}$, 0.25/>4 µg/mL) against 954 *P. aeruginosa* isolates (**Table 2**).
  - JNJ-Q2 demonstrated excellent activity ($MIC_{50/90}$, 1/2 µg/mL) against *Acinetobacter* spp. being clearly more active than ciprofloxacin, moxifloxacin, and levofloxacin, each with MIC_{50}, >4 µg/mL (**Table 2**). JNJ-Q2 had similar activity to the two most active agents; tigecycline and colistin ($MIC_{50/90}$, 1/2 µg/mL for both agents) with high resistance rates found for all other agents tested (**Table 2**).
  - JNJ-Q2 demonstrated modest activity ($MIC_{50/90}$, 0.5/4 µg/mL) against 157 *S. maltophilia* tested (**Table 1**).

Table 1. MIC frequency and cumulative percent inhibited distributions of JNJ-Q2 by species and/or organism group

	No. of isolates (cumulative %) inhibited at MIC (µg/mL):														
Organism (no. tested)	≤0.002	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4	MIC_{50}	MIC_{90}
Streptococcus pneumoniae (2,162)	2 (0.1)	17 (0.9)	646 (30.8)	1412 (96.1)	59 (98.8)	17 (99.6)	8 (>99.9)	1 (100.0)	--	--	--	--	--	0.015	0.015
Haemophilus influenzae (1,295)	25 (1.9)	317 (26.4)	533 (67.6)	299 (90.7)	89 (97.5)	23 (99.3)	4 (99.6)	3 (99.8)	1 (99.9)	1 (100.0)	--	--	--	0.008	0.015
Moraxella catarrhalis (505)	1 (0.2)	2 (0.6)	84 (17.2)	397 (95.8)	20 (99.8)	1 (100.0)	--	--	--	--	--	--	--	0.015	0.015
Staphylococcus aureus (4,537)	40 (0.9)	997 (22.9)	1616 (58.5)	374 (66.7)	48 (67.8)	74 (69.4)	655 (83.8)	570 (96.4)	84 (98.3)	67 (99.7)	12 (100.0)	--	--	0.008	0.25
levofloxacin-intermediate (43)	--	--	2 (4.7)	3 (11.6)	12 (39.5)	22 (90.7)	4 (100.0)	--	--	--	--	--	--	0.06	0.06
MRSA, levofloxacin-susceptible (424)	1 (0.2)	95 (22.6)	266 (85.4)	53 (97.9)	7 (99.5)	0 (99.5)	2 (100.0)	--	--	--	--	--	--	0.008	0.015
MSSA, levofloxacin-susceptible (2,643)	39 (1.5)	902 (35.6)	1347 (86.6)	318 (98.6)	24 (99.5)	9 (99.8)	4 (100.0)	--	--	--	--	--	--	0.008	0.015
MRSA, levofloxacin-resistant (1,247)	--	--	1 (0.1)	0 (0.1)	2 (0.2)	35 (3.0)	540 (46.4)	519 (88.0)	78 (94.2)	60 (99.0)	12 (100.0)	--	--	0.25	0.5
MSSA, levofloxacin-resistant (180)	--	--	--	--	3 (1.7)	8 (6.1)	105 (64.4)	51 (92.8)	6 (96.1)	7 (100.0)	--	--	--	0.12	0.25
β-haemolytic streptococci (1,145)	--	6 (0.5)	376 (33.4)	661 (91.1)	79 (98.0)	3 (98.3)	18 (99.8)	2 (100.0)	--	--	--	--	--	0.015	0.015
Viridans group streptococci (606)	14 (2.3)	36 (8.3)	231 (46.4)	269 (90.8)	30 (95.7)	14 (98.0)	5 (98.8)	6 (99.8)	1 (100.0)	--	--	--	--	0.015	0.015
Enterococcus spp. (853)	--	--	1 (0.1)	9 (1.2)	91 (11.8)	289 (45.7)	21 (48.2)	45 (53.5)	128 (68.5)	91 (79.1)	143 (95.9)	34 (99.9)	1 (100.0)	0.25	2
vancomycin-susceptible (690)	--	--	1 (0.1)	9 (1.4)	90 (14.5)	289 (56.4)	21 (59.4)	39 (65.1)	111 (81.2)	63 (90.3)	57 (98.6)	9 (99.9)	1 (100.0)	0.06	1
vancomycin-non-susceptible (163)	--	--	--	--	1 (0.6)	0 (0.6)	0 (0.6)	6 (4.3)	17 (14.7)	28 (31.9)	86 (84.7)	25 (100.0)	--	2	4
Escherichia coli (1,391)	--	1 (0.1)	32 (2.4)	263 (21.3)	404 (50.3)	107 (58.0)	86 (64.2)	46 (67.5)	18 (68.8)	72 (74.0)	241 (91.3)	96 (98.2)	25 (100.0)	0.03	2
non-ESBL-phenotype (1,076)	--	1 (0.1)	31 (3.0)	249 (26.1)	386 (62.0)	101 (71.4)	70 (77.9)	34 (81.0)	10 (82.0)	33 (85.0)	110 (95.3)	43 (99.3)	8 (100.0)	0.03	2
ESBL-phenotype (315)	--	--	1 (0.3)	14 (4.8)	18 (10.5)	6 (12.4)	16 (17.5)	12 (21.3)	8 (23.8)	39 (36.2)	131 (77.8)	53 (94.6)	17 (100.0)	2	4
Klebsiella spp. (896)	--	--	1 (0.1)	3 (0.4)	126 (14.5)	352 (53.8)	65 (61.0)	48 (66.4)	61 (73.2)	68 (80.8)	57 (87.2)	44 (92.1)	71 (100.0)	0.06	4
Klebsiella pneumoniae (772)	--	--	1 (0.1)	3 (0.5)	91 (12.3)	285 (49.2)	59 (56.9)	42 (62.3)	58 (69.8)	63 (78.0)	55 (85.1)	44 (90.8)	71 (100.0)	0.12	4
non-ESBL-phenotype (498)	--	--	1 (0.2)	3 (0.8)	86 (18.1)	268 (71.9)	54 (82.7)	26 (88.0)	23 (92.6)	9 (94.4)	8 (96.0)	8 (97.6)	12 (100.0)	0.06	0.5
ESBL-phenotype (274)	--	--	--	--	5 (1.8)	17 (8.0)	5 (9.9)	16 (15.7)	35 (28.5)	54 (48.2)	47 (65.3)	36 (78.5)	59 (100.0)	2	>4
Proteus mirabilis (225)	--	--	--	--	3 (1.3)	40 (19.1)	95 (61.3)	20 (70.2)	7 (73.3)	21 (82.7)	14 (88.9)	8 (92.4)	17 (100.0)	0.12	4
Citrobacter spp. (176)	--	1 (0.6)	0 (0.6)	15 (9.1)	44 (34.1)	38 (55.7)	9 (60.8)	19 (71.6)	17 (81.3)	12 (88.1)	10 (93.8)	5 (96.6)	6 (100.0)	0.06	2
Enterobacter spp. (430)	--	--	--	2 (0.5)	43 (10.5)	195 (55.8)	79 (74.2)	16 (77.9)	19 (82.3)	30 (89.3)	11 (91.9)	14 (95.1)	21 (100.0)	0.06	2
Indole-positive proteus spp. (187)	--	--	--	--	8 (4.3)	44 (27.8)	49 (54.0)	16 (62.6)	14 (70.1)	15 (78.1)	17 (87.2)	18 (96.8)	6 (100.0)	0.12	4
Serratia spp. (238)	--	--	--	1 (0.4)	4 (2.1)	4 (3.8)	23 (13.4)	83 (48.3)	82 (82.8)	20 (91.2)	9 (95.0)	2 (95.8)	10 (100.0)	0.5	1
Pseudomonas aeruginosa (954)	--	--	--	1 (0.1)	4 (0.5)	4 (0.9)	10 (2.0)	122 (14.8)	334 (49.8)	123 (62.7)	92 (72.3)	80 (80.7)	184 (100.0)	1	>4
Acinetobacter spp. (419)	--	--	9 (2.1)	40 (11.7)	26 (17.9)	11 (20.5)	6 (22.0)	25 (27.9)	62 (42.7)	118 (70.9)	91 (92.6)	27 (99.0)	4 (100.0)	1	2
Stenotrophomonas maltophilia (157)	--	--	--	--	--	--	11 (7.0)	32 (27.4)	41 (53.5)	39 (78.3)	16 (88.5)	13 (96.8)	5 (100.0)	0.5	4

Table 2. Antimicrobial activity of JNJ-Q2 and comparator antimicrobials against pathogens

Organism (no. tested)/ Antimicrobial agent[a]	MIC in µg/mL 50%	90%	Range	CLSI[b] %S / %I / %R	EUCAST[b] %S / %I / %R
S. pneumoniae (2,162)					
JNJ-Q2	0.015	0.015	≤0.002 – 0.25	-[c] / - / -	- / - / -
Moxifloxacin	≤0.12	0.25	≤0.12 – >4	99.0 / 0.6 / 0.4	98.8 / 0.1 / 1.3
Levofloxacin	1	1	≤0.12 – >4	98.6 / 0.2 / 1.2	98.6 / 0.0 / 1.4
Ciprofloxacin	1	2	0.06 – >4	- / - / -	0.1 / 94.8 / 5.1
Penicillin[d]	≤0.06	2	≤0.06 – >8	91.3 / 7.4 / 1.3	- / -
Penicillin[e]	≤0.06	2	≤0.06 – >8	62.0 / 20.5 / 17.5	62.0 / 29.3 / 8.7
Amoxicillin/clavulanate	≤1	4	≤1 – >8	88.7 / 3.1 / 8.2	- / - / -
Ceftriaxone	≤0.06	1	≤0.06 – 8	90.1 / 8.0 / 1.9	80.6 / 17.5 / 1.9
Cefuroxime	≤0.5	8	≤0.5 – >16	88.5 / 0.0 / 11.5	86.9 / 1.6 / 11.5
Tetracycline	≤0.25	>8	≤0.25 – >8	72.3 / 1.1 / 26.6	71.9 / 0.4 / 27.7
TMP/SMX[f]	≤0.5	>4	≤0.5 – >4	66.6 / 12.0 / 21.4	73.2 / 5.4 / 21.4
Clindamycin	≤0.25	>2	≤0.25 – >2	78.4 / 0.6 / 21.0	79.0 / 0.0 / 21.0
Linezolid	1	1	≤0.12 – 2	100.0 / - / -	100.0 / 0.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 0.5	100.0 / - / -	100.0 / 0.0 / 0.0
Erythromycin	≤0.12	>16	≤0.12 – >16	62.7 / 0.6 / 36.7	62.7 / 0.6 / 36.7
H. influenzae (1,295)					
JNJ-Q2	0.008	0.015	≤0.002 – 1	- / - / -	- / - / -
Ciprofloxacin	≤0.03	≤0.03	≤0.03 – >4	99.8 / - / -	99.5 / 0.0 / 0.5
Moxifloxacin	≤0.12	≤0.12	≤0.12 – 4	99.8 / - / -	99.8 / 0.0 / 0.2
Levofloxacin	≤0.12	≤0.12	≤0.12 – >4	99.8 / - / -	99.8 / 0.0 / 0.2
Ampicillin	≤0.25	>8	≤0.25 – >8	78.7 / 1.8 / 19.5	78.7 / 0.0 / 21.3
Amoxicillin/clavulanate	≤1	2	≤1 – 8	99.5 / 0.0 / 0.5	98.3 / 0.0 / 1.7
Ceftriaxone	≤0.06	≤0.06	≤0.06 – 0.5	100.0 / - / -	99.5 / 0.0 / 0.5
Cefuroxime	1	2	≤0.12 – >16	98.2 / 0.9 / 0.9	75.6 / 17.3 / 7.1
Tetracycline	0.5	1	≤0.12 – >16	98.4 / 0.0 / 1.6	98.1 / 0.3 / 1.6
Tigecycline[g]	0.25	0.5	0.06 – 2	85.3 / - / -	- / - / -
TMP/SMX	≤0.5	>4	≤0.5 – >4	65.8 / 5.0 / 29.2	65.8 / 2.7 / 31.5
Azithromycin	1	2	≤0.03 – >4	98.9 / - / -	0.7 / 98.2 / 1.1
Clarithromycin	8	16	≤0.12 – >16	90.0 / 8.6 / 1.4	1.0 / 97.6 / 1.4
M. catarrhalis (505)					
JNJ-Q2	0.015	0.015	≤0.002 – 0.06	- / - / -	- / - / -
Ciprofloxacin	≤0.03	0.06	≤0.03 – 1	100.0 / - / -	99.8 / 0.0 / 0.2
Moxifloxacin	≤0.12	≤0.12	≤0.12 – 0.5	- / - / -	100.0 / 0.0 / 0.0
Levofloxacin	≤0.12	≤0.12	≤0.12 – 1	100.0 / - / -	100.0 / 0.0 / 0.0
Penicillin	>2	>2	≤0.03 – >2	- / - / -	- / - / -
Amoxicillin/clavulanate	≤1	≤1	≤1	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Imipenem	≤0.12	≤0.12	≤0.12	- / - / -	100.0 / 0.0 / 0.0
Ceftriaxone	0.25	0.5	≤0.06 – 4	99.8 / - / -	99.6 / 0.2 / 0.2
Cefuroxime	≤0.5	-	≤0.5	100.0 / 0.0 / 0.0	100.0 / 0.0 / 0.0
Tetracycline	0.25	0.25	≤0.12 – 8	99.8 / 0.0 / 0.2	99.8 / 0.0 / 0.2
Tigecycline[g]	0.06	0.06	≤0.015 – 0.12	- / - / -	- / - / -
TMP/SMX	≤0.5	≤0.5	≤0.5 – 4	93.3 / 5.9 / 0.8	93.3 / 3.7 / 3.0
Azithromycin	≤0.03	0.06	≤0.03 – >4	99.2 / - / -	99.4 / 0.0 / 0.6
S. aureus (4,537)					
JNJ-Q2	0.008	0.25	≤0.002 – 2	- / - / -	- / - / -
Moxifloxacin	≤0.12	4	≤0.12 – >4	68.2 / 10.0 / 21.8	68.2 / 10.0 / 21.8
Levofloxacin	0.25	>4	≤0.12 – >4	67.6 / 0.9 / 31.5	67.6 / 0.9 / 31.5
Ciprofloxacin	0.5	>4	≤0.03 – >4	66.1 / 1.4 / 32.5	66.1 / 0.0 / 33.9
Erythromycin	0.25	>16	≤0.12 – >16	55.0 / 2.0 / 43.0	55.4 / 0.4 / 44.2
Clindamycin	≤0.25	>2	≤0.25 – >2	83.4 / 0.2 / 16.4	83.1 / 0.3 / 16.6
Daptomycin	0.25	0.5	≤0.06 – 2	>99.9 / - / -	>99.9 / 0.0 / <0.1
Vancomycin	1	1	0.25 – 4	>99.9 / <0.1 / 0.0	>99.9 / 0.0 / <0.1
Linezolid	1	2	≤0.12 – 8	>99.9 / 0.0 / <0.1	>99.9 / 0.0 / <0.1
Oxacillin	0.5	>2	≤0.25 – >2	62.7 / 0.0 / 37.3	62.7 / 0.0 / 37.3
Ceftriaxone	4	>8	0.5 – >8	62.7 / 0.0 / 37.3	62.7 / 0.0 / 37.3
Tigecycline[g]	0.06	0.12	≤0.03 – 0.5	100.0 / - / -	100.0 / 0.0 / 0.0
Tetracycline	≤0.25	8	≤0.25 – >8	89.7 / 0.7 / 9.6	88.9 / 0.5 / 10.6
TMP/SMX	≤0.5	≤0.5	≤0.5 – >4	98.7 / 0.0 / 1.3	98.7 / 0.2 / 1.1
β-hemolytic streptococci (1,145)					
JNJ-Q2	0.015	0.015	0.004 – 0.25	- / - / -	- / - / -
Moxifloxacin	≤0.12	0.25	≤0.12 – >4	- / - / -	98.0 / 0.1 / 1.9
Levofloxacin	0.5	1	≤0.12 – >4	97.9 / 0.2 / 1.9	94.5 / 3.4 / 2.1
Penicillin	≤0.06	≤0.06	≤0.06 – 0.12	100.0 / - / -	100.0 / 0.0 / 0.0
Erythromycin	≤0.12	>16	≤0.12 – >16	75.4 / 0.9 / 23.7	75.4 / 0.9 / 23.7
Clindamycin	≤0.25	>2	≤0.25 – >2	87.6 / 0.5 / 11.9	88.1 / 0.0 / 11.9
Linezolid	1	1	0.25 – 2	100.0 / - / -	100.0 / 0.0 / 0.0
TMP/SMX	≤0.5	≤0.5	≤0.5 – >4	- / - / -	97.8 / 0.5 / 1.7
Daptomycin	≤0.06	0.25	≤0.06 – 0.5	100.0 / - / -	100.0 / 0.0 / 0.0
Vancomycin	0.25	0.5	≤0.12 – 1	100.0 / - / -	100.0 / 0.0 / 0.0
Viridans group streptococci (606)					
JNJ-Q2	0.015	0.015	≤0.002 – 0.5	- / - / -	- / - / -
Levofloxacin	1	2	≤0.12 – >4	94.7 / 1.2 / 4.1	- / - / -
Penicillin	≤0.06	1	≤0.06 – >4	75.9 / 20.6 / 3.5	83.0 / 13.5 / 3.5
Erythromycin	≤0.12	>16	≤0.12 – >16	54.3 / 2.5 / 43.2	- / - / -
Clindamycin	≤0.25	>2	≤0.25 – >2	86.3 / 0.8 / 12.9	87.1 / 0.0 / 12.9
Linezolid	1	1	≤0.12 – 2	100.0 / - / -	- / - / -
Daptomycin	0.25	0.5	≤0.06 – 4	99.8 / - / -	- / - / -
Vancomycin	0.5	1	≤0.12 – 1	100.0 / - / -	100.0 / 0.0 / 0.0
Enterococcus spp. (853)					
JNJ-Q2	0.25	2	0.008 – >4	- / - / -	- / - / -
Levofloxacin	>4	>4	0.25 – >4	48.2 / 1.6 / 50.2	- / - / -
Ciprofloxacin	>4	>4	0.25 – >4	40.6 / 6.8 / 52.6	- / - / -
Ampicillin	1	>8	≤0.25 – >8	67.3 / 0.0 / 32.7	66.0 / 1.3 / 32.7
Tigecycline[g]	≤0.03	0.06	≤0.03 – 0.25	100.0 / - / -	100.0 / 0.0 / 0.0
Tetracycline	>8	>8	≤0.25 – >8	29.5 / 1.3 / 69.2	- / - / -
TMP/SMX	≤0.5	>4	≤0.5 – >4	- / - / -	52.0 / 0.3 / 47.7
Vancomycin	1	>16	0.25 – >16	80.9 / 0.5 / 18.6	80.9 / 0.0 / 19.1
Teicoplanin	≤2	>16	≤2 – >16	82.6 / 1.7 / 15.7	82.2 / 0.0 / 17.8
Linezolid	1	2	0.25 – 4	99.6 / 0.4 / 0.0	100.0 / 0.0 / 0.0
Daptomycin	1	2	≤0.06 – >4	99.9 / - / -	- / - / -
Enterobacteriaceae[h] (3,543)					
JNJ-Q2	0.12	2	0.004 – >4	- / - / -	- / - / -
Ciprofloxacin	≤0.03	>4	≤0.03 – >4	74.5 / 2.3 / 23.2	72.2 / 2.3 / 25.5
Moxifloxacin	≤0.12	>4	≤0.12 – >4	- / - / -	68.8 / 3.3 / 27.9
Levofloxacin	≤0.12	>4	≤0.12 – >4	77.4 / 2.8 / 19.8	75.4 / 2.0 / 22.6
Ampicillin	>8	>8	0.5 – >8	21.2 / 0.0 / 78.8	21.2 / 0.0 / 78.8
Amoxicillin/clavulanate	8	>8	≤1 – >8	54.2 / 0.0 / 45.8	54.2 / 0.0 / 45.8
Ceftazidime	0.25	32	≤0.015 – >32	81.3 / 3.0 / 15.7	77.0 / 4.3 / 18.7
Aztreonam	≤0.12	>16	≤0.12 – >16	79.8 / 2.2 / 18.0	76.7 / 5.3 / 18.0
Ceftriaxone	0.12	>8	≤0.06 – >8	75.4 / 0.8 / 23.8	75.4 / 0.8 / 23.8
Cefepime	≤0.5	>16	≤0.5 – >16	86.6 / 2.2 / 11.2	80.1 / 4.2 / 15.7
Imipenem	≤0.12	2	≤0.12 – >8	89.9 / 6.9 / 3.2	96.8 / 1.8 / 1.4
Tigecycline[g]	0.25	1	0.03 – 4	98.3 / 1.7 / 0.0	93.6 / 4.7 / 1.7
Tetracycline	2	>8	0.5 – >8	59.0 / 3.4 / 37.6	- / - / -
Gentamicin	≤1	>8	≤1 – >8	84.2 / 1.0 / 14.8	82.8 / 1.4 / 15.8
TMP/SMX	≤0.5	>4	≤0.5 – >4	70.7 / 0.0 / 29.3	70.7 / 0.8 / 28.5
Colistin	0.5	>4	≤0.25 – >4	- / - / -	78.9 / 0.0 / 21.1
P. aeruginosa (954)					
JNJ-Q2	1	>4	0.015 – >4	- / - / -	- / - / -
Ciprofloxacin	0.25	>4	≤0.03 – >4	71.4 / 4.4 / 24.2	67.0 / 4.4 / 28.6
Moxifloxacin	2	>4	≤0.12 – >4	- / - / -	- / - / -
Levofloxacin	0.5	>4	≤0.12 – >4	70.0 / 4.8 / 25.2	62.6 / 7.4 / 30.0
Piperacillin/tazobactam	8	>64	≤0.5 – >64	68.5 / 14.6 / 16.9	68.5 / 0.0 / 31.5
Ceftazidime	2	>32	0.06 – >32	74.3 / 6.0 / 19.7	74.3 / 0.0 / 25.7
Aztreonam	8	>16	≤0.12 – >16	65.5 / 12.2 / 22.3	3.6 / 74.1 / 22.3
Imipenem	1	>8	≤0.12 – >8	69.3 / 4.9 / 25.8	74.2 / 11.2 / 14.6
Tigecycline	4	>4	0.06 – >4	- / - / -	- / - / -
Tetracycline	>8	>8	0.5 – >8	10.5 / 35.8 / 53.7	- / - / -
Amikacin	2	16	≤0.25 – >32	90.6 / 2.3 / 7.1	87.2 / 3.4 / 9.4
Tobramycin	0.5	>16	≤0.12 – >16	86.1 / 0.8 / 13.1	86.1 / 0.0 / 13.9
TMP/SMX	4	>4	≤0.5 – >4	15.2 / 0.0 / 84.8	- / - / -
Colistin	1	2	≤0.25 – >8	99.6 / 0.2 / 0.2	99.6 / 0.0 / 0.4
A. baumannii (419)					
JNJ-Q2	1	2	0.008 – >4	- / - / -	- / - / -
Ciprofloxacin	>4	>4	0.06 – >4	21.2 / 0.0 / 78.8	21.2 / 0.0 / 78.8
Moxifloxacin	>4	>4	≤0.12 – >4	- / - / -	- / - / -
Levofloxacin	>4	>4	≤0.12 – >4	21.7 / 5.5 / 72.8	21.2 / 0.5 / 78.3
Piperacillin/tazobactam	>64	>64	≤0.5 – >64	22.4 / 0.0 / 77.6	- / - / -
Ceftazidime	>32	>32	0.5 – >32	24.1 / 2.6 / 73.3	- / - / -
Aztreonam	>16	>16	4 – >16	3.1 / 10.5 / 86.4	- / - / -
Imipenem	>8	>8	≤0.12 – >8	31.3 / 3.3 / 65.4	28.6 / 6.0 / 65.4
Tigecycline	1	2	0.03 – 8	- / - / -	- / - / -
Tetracycline	32	>32	0.25 – >32	28.9 / 10.3 / 60.8	- / - / -
Amikacin	>32	>32	1 – >32	38.4 / 3.1 / 58.5	34.6 / 3.8 / 61.6
Tobramycin	>16	>16	≤0.12 – >16	40.0 / 4.6 / 55.4	40.0 / 0.0 / 60.0
TMP/SMX	>4	>4	≤0.5 – >4	33.0 / 0.0 / 67.0	33.0 / 2.9 / 64.1
Colistin	1	2	0.25 – >8	96.9 / 0.0 / 3.1	96.9 / 0.0 / 3.1
S. maltophilia (157)					
JNJ-Q2	0.5	4	0.12 – >4	- / - / -	- / - / -
Ciprofloxacin	2	>4	0.25 – >4	- / - / -	- / - / -
Moxifloxacin	0.5	4	≤0.12 – >4	- / - / -	- / - / -
Levofloxacin	1	4	0.25 – >4	83.4 / 7.7 / 8.9	- / - / -
Piperacillin/tazobactam	>64	>64	8 – >64	- / - / -	- / - / -
Ceftazidime	16	>32	1 – >32	39.4 / 10.9 / 49.7	- / - / -
Aztreonam	>16	>16	4 – >16	- / - / -	- / - / -
Imipenem	>8	>8	8 – >8	- / - / -	- / - / -
Tigecycline	0.5	2	0.06 – 4	- / - / -	- / - / -
Tetracycline	16	32	2 – >32	- / - / -	- / - / -
Amikacin	>32	>32	4 – >32	- / - / -	- / - / -
Tobramycin	>16	>16	2 – >16	- / - / -	- / - / -
TMP/SMX	≤0.5	1	≤0.5 – >4	94.3 / 0.0 / 5.7	96.2 / 0.0 / 3.8
Colistin	4	>8	0.25 – >8	- / - / -	- / - / -

a. S = susceptible, I = intermediate, R = resistant.
b. Criteria as published by the CLSI [2013] and EUCAST [2013].
c. A dash indicates no breakpoint criteria have currently been established.
d. Criteria as published by the CLSI [2013] for 'Penicillin parenteral non-meningitis' (S≤2, I=4, R≥8 µg/mL).
e. Criteria as published by the CLSI [2013] for 'Penicillin oral penicillin V' (S ≤0.06, I=0.12‑1, R≥2 µg/mL).
f. Trimethoprim/sulfamethoxazole.
g. US-FDA breakpoints were applied [Tygacil Product Insert, 2012].
h. Includes: *C. amalonaticus* (four strains), *C.braakii* (six strains), *C. farmeri* (one strain), *C. freundii* (82 strains), *C. koseri* (66 strains), *C. sedlakii* (one strain), *C. youngae* (one strain), *E. aerogenes* (129 strains), *E. asburiae* (three strains), *E. cloacae* (294 strains), *E. sakazakii* (one strain), *E. coli* (1391 strains), *K. oxytoca* (124 strains), *K. pneumoniae* (772 strains), *M. morganii* (187 strains), *P. mirabilis* (225 strains), *S. liquefaciens* (seven strains), *S. marcescens* (231 strains), unspeciated *Citrobacter* (15 strains), and unspeciated *Enterobacter* (three strains).

CONCLUSIONS

- JNJ-Q2 demonstrated excellent activity when tested against a global collection of 2012 CABP pathogens, including the most prevalent pathogen *S. pneumoniae.* Nearly all isolates (>99.9%) of pneumococci were inhibited at a MIC of ≤0.12 µg/mL. JNJ-Q2 also demonstrated excellent activity against *H. influenzae* and *M. catarrhalis*.
- JNJ-Q2 exhibited good activity overall against this global collection of *S. aureus*, >98% of the isolates were inhibited at ≤0.5 µg/mL. The potency of JNJ-Q2 was observed to be less in levofloxacin-resistant strains compared to levofloxacin-susceptible strains with a MIC_{90} of 0.5 µg/mL for MRSA and 0.25 µg/mL for MSSA. JNJ-Q2 demonstrated excellent activity against β-haemolytic and viridans streptococci and good *in vitro* activity *Enterococcus* spp.
- JNJ-Q2 showed good *in vitro* activity against Enterobacteriaceae but was less active against ESBL-phenotypes than non-ESBL-phenotypes which was directly related to the prevalence of ciprofloxacin resistance in the ESBL subpopulation. JNJ-Q2 also demonstrated good activity against *Acinetobacter* spp. being clearly more active than ciprofloxacin, moxifloxacin and levofloxacin and having similar activity to the two most active agents; tigecycline and colistin.
- These favorable results support the further clinical development of JNJ-Q2 to treat CABP and ABSSSI and selected multi-resistant pathogens.

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