

Update in infection related meetings 2018

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Highlights at the ASM Microbe 2018, Atlanta (USA)

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INTRODUCTION

The meeting of the American Society for Microbiology, ASM Microbe, is a huge meeting that includes all disciplines of Microbiology, from basic science to clinical aspects [1]. The last ASM Microbe held in Atlanta (USA) last June 2018, included current trends regarding antimicrobial agents and resistance, applied and environmental science, clinical infections and vaccines, clinical and public health microbiology, host-microbe biology, microbial ecology and evolution, molecular biology and physiology, and profession of microbiology. There were 24 plenary sessions, 84 symposia, 25 meet-the-expert sessions, 20 workshops, and more than 2000 abstracts were presented as poster presentations or poster talks. Since it is not possible to summarize in a few pages all the aspects covered in this meeting, this minireview will try to summarize, some of the contributions related to microbiological diagnosis, resistance to antimicrobials, and new antimicrobials.

DIAGNOSTIC MICROBIOLOGICAL TECHNIQUES

Over the past decade, the field of clinical microbiology has experienced a significant development due to new technologies that have improved the diagnosis of infectious diseases. Sensitive diagnostic tests that can be performed at the site of patient care (point-of-care testing) with minimal infrastructure, cost, and training, provide a decrease of the time between sample collection and diagnosis [2]. In this setting, loop-mediated isothermal amplification (LAMP) assays can be used as point of care tests. One study presented at this meeting evaluates the diagnostic performance of a LAMP assay combined with lateral flow dipstick (LFD) as point of care method for the diagnosis

of tuberculosis (Nimesh M, et al; abstract 6074). The assay, standardized to detect simultaneously the *Mycobacterium tuberculosis sdaA* gene and the rifampicin resistance gene *rpoB*, was tested in 18 culture confirmed specimens for pulmonary tuberculosis. All the specimens showed a positive result with LAMP-LFD assay. The diagnostic accuracy of the method was also evaluated in comparison with GeneXpert MTB/RIF assay (3) using 107 clinical specimens from patients with clinical symptoms of pulmonary tuberculosis. Out of 107, 15 specimens were positive with both methods showing high concordance and accuracy in comparison to other methods.

Another study evaluates a LAMP assay (TangenDX™ system) for direct detection of *Candida* species from blood (Zanini A, et al; abstract 5352). The assay detects 5 species of *Candida*. After analyzing 43 spiked blood samples, *Candida* species were detected correctly in 96.1% at a pathogen concentration of 2–3 cfu/ml of whole blood. Sample processing time was 5–7 minutes and time to positive results was 70 minutes. The high sensitivity and the small size of this portable device, make this a reliable diagnostic test.

MALDI-TOF mass spectrometry can be used to perform antimicrobial susceptibility testing by the detection of drug hydrolysis. In addition, this system can also detect resistant strains by peak picking approaches [4]. Two studies aimed to detect specific peaks associated with resistance. In one of them MALDI-TOF MS was able to discriminate between vancomycin-resistant *Enterococcus faecium* (VREfm; 91 strains) and vancomycin-susceptible *E. faecium* (VSEfm; 31 strains). Overall, 30 peaks ranging from 2,212 to 10,225 m/z were detected, and 12 of these were exclusively associated with VREfm: four of them were present in 100% and eight were present in more than 90% of the 91 VREfm strains and absent in all 31 VSEfm isolates, demonstrating the ability to discriminate between VREfm and VSEfm isolates (Ribeiro RL, et al; abstract 6119). Other study (Cordovana M, et al; abstract 6403), based on the detection of the carbapenemase KPC-specific peak at 11,109 m/z in the MALDI-TOF MS spectra of *K. pneumoniae*, developed

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specific algorithms for automated detection of KPC-producing enterobacteria (*E. coli*, *Enterobacter* spp., *K. oxytoca*, *Citrobacter* spp., and *S. marcescens*), showing a high sensitivity (85%) and excellent specificity (99.9%).

Whole-organism fingerprinting by attenuated total reflectance-Fourier transform infrared (ATR-FTIR) spectroscopy is a rapid (1 minute), reagent-free technique for bacterial identification and classification with subspecies-level discriminatory capabilities [5]. In one study, by analyzing 93 vancomycin-resistant *E. faecium* (VRE) from two clonal groups, according to PFGE typing, the ATR-FTIR spectroscopy was able to classify the organisms as antibiotic resistant, and showed successful discrimination between two VRE clonal groups, yielding 99% concordance with PFGE results. The authors concluded that this technique, that is performed with a portable instrument, can be easily implemented as a typing method suitable for intrahospital surveillance of VRE outbreaks (Tsutsumi T, et al; abstract 8868). The ATR-FTIR spectroscopy was also applied in other study for the discrimination between fluconazole-resistant and fluconazole-susceptible *Candida auris*, and for the discrimination between *C. auris*, *C. haemulonii* and *C. duobushaemulonii* with 100% correct classification at the species level in comparison with reference methods and discrimination between fluconazole-susceptible and resistant strains (Lam L, et al; abstract 8961).

Multiplex molecular tests represent an advancement for rapidly and reliably detect and identify causes of infectious diseases. Among these, the syndromic microarray-based nucleic acid assays have shown high positive-predictive values for detection of organisms in blood, CSF, stool, and respiratory samples [6]. Several studies presented at the ASM Microbe have assessed the performance of syndromic PCR panels (FilmArray, Biofire, bioMérieux) for the diagnosis of gastroenteritis, meningitis, and pneumonia, and have evaluated its clinical impact. In a prospective, multi-center study, the authors investigate the impact of a gastrointestinal panel on clinical diagnosis and decision-making, and compared the clinical acuity of patients with positive results obtained exclusively with the panel versus those detected by conventional stool culture. The panel detected a pathogen in 35.3% (669/1,887) of specimens, compared to 6.0% (113/1,887) detected by stool culture. The median time from collection to result was 18 h for the panel compared with 47 h for stool culture. The median time from collection to initiation of appropriate antimicrobial therapy was 22 h for the panel compared with 72 h for stool culture, indicating that the use of the syndromic panel can substantially increase the speed and sensitivity of laboratory diagnosis and inform clinical decisions in patients with acute gastroenteritis (Bateman A, et al; abstract 6215). In a study that performed a total of 216 tests in CSF with the FilmArray meningitis-encephalitis panel and in which they also collected white blood cell counts (WBC), 14 specimens (6.5%) were positive, and all samples with normal WBC were negative. The panel improved the ability to provide rapid PCR results for 14 infectious agents and improved the turnaround to a few hours. The authors suggest that the panel should not be performed in

samples that have normal WBC counts (Bolster LaSalle CM, et al; abstract 4565). Another study assessed the clinical impact of a respiratory panel when used as a point-of-care test (results in 1 h) in an urgent care setting (Mortimer L, et al; abstract 6280). A total of 98 patients were enrolled with a syndromic panel and 53 tested positive (54%), with 51 testing positive for a viral pathogen (96%) and 2 for a bacterial pathogen (4%). The use of this panel decreased the time to which actionable results were available and improved antimicrobial stewardship. Finally, a multi-center evaluation (8 USA sites) was conducted in order to establish the clinical performance of the Biofire Filmarray® Pneumonia Panel Plus (investigational use only version of the assay). This panel detects 18 bacteria (15 with semi-quantitation), 9 viruses, and 7 antibiotic resistance markers. The overall positive and negative agreement was 93.6% and 99.2%, respectively, compared to the reference methods. For analytes reported with semi-quantitation, the panel demonstrated essential agreement with the correct log bin value +/- 1 bin 97.7% of the time as compared to qNGS, demonstrating that it is a sensitive and specific test for detection of pathogens in sputum and bronchoalveolar lavage (BAL) (Kerr S, et al; abstract 4266).

Magnetic resonance is among the new technologies developed for detecting microorganisms in clinical samples [7]. The T2Bacteria panel, is a novel nanodiagnostic panel that uses T2 magnetic resonance and a dedicated instrument to detect as few as 1-10 cfu/mL of six different organisms (*A. baumannii*, *E. faecium*, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *S. aureus*) directly in whole blood with results in 3-5 hours. In a multicenter prospective study (Nguyen M, et al; abstract 7975), the T2Bacteria panel was compared with blood cultures (BC) for diagnosing bacteremia. A total of 1,427 BC were tested, and the T2Bacteria sensitivity and specificity based on BC results were 90% and 88%, respectively; four samples had T2-/BC+ and 176 samples from 168 patients had T2+/BC- results (24% from patients who had received previous antimicrobial therapy, 23% from patients with positive BC for the same species within the 21 preceding days, 16% from patients with positive non-blood site cultures in the preceding 14 days, 19% from patients with presumed infection but either BC were not drawn or negative, and the remaining were considered false positive results). In summary, the panel demonstrated good performance in detecting bacteremia with lower time to test positivity in comparison with BC, and potential for diagnosing deep-seated infections.

Laser light-scattering is a technology that has been used for the rapid detection of bacterial growth in human specimens and in the screening of urine specimens to facilitate the diagnosis of urinary tract infections. The BacterioScan 216Dx, is a laser light-scattering instrument, that can be used with urine and with BAL specimens. In one study, the authors determined the improvement in performance of this instrument compared to standard methods (Tomaras A, et al; abstract 5577). A total of 55 BAL specimens were analyzed by first diluting them into brain heart infusion broth and subsequently incubating them in the 216Dx for 20 hours, during which optical

measurements were collected every 3–5 minutes. Considering clinically significant bacterial counts of $\geq 10,000$ cfu/mL, 25% of BAL specimens were positive by conventional culture, and the 216Dx demonstrated sensitivity and specificity values of 85.7% and 87.8%, respectively, at 6 h, and 92.9% and 73.2%, respectively, at 8 h, showing that this method can be used as a screening method for BAL specimens with clinically-relevant densities of respiratory pathogens. Laser light-scattering can also be used for rapid antimicrobial susceptibility testing (AST) directly from urine samples. One study presented at this meeting compared the susceptibility results obtained with the 216Dx directly from urine samples, to MIC reports (Vitek 2, bioMerieux; gold standard) from urine culture isolates for 4 antimicrobials (ciprofloxacin, ceftriaxone, ceftazidime, and meropenem) against Gram-negative pathogens. Positive urine samples were diluted in Mueller-Hinton broth and inoculated to antibiotic cuvettes of the 216Dx. A total of 112 AST were performed and the concordance with the standard for all 4 drugs was 94.4%, with 3 minor errors, 1 major error, and 1 very major error. Results were available within 4 hours, confirming that this technology provides early phenotypic evidence of antimicrobial susceptibility and resistance (Riederer KM, et al; abstract 8903).

Peptide nucleic acid fluorescence *in situ* hybridization (PNA-FISH) is a technology that has been used for the direct detection of bacteria, fungi, and parasites in clinical samples [8]. In one study, the authors evaluated the use of a simple and inexpensive dual-colour fluorescence *in situ* hybridization assay for identifying *Plasmodium knowlesi*. Methanol fixed thin blood smears were hybridized with two fluorescent labeled probes: *Plasmodium* genus and *P. knowlesi* specific probe at 37°C for 15 minutes. The limit of detection in the *P. knowlesi* FISH assay was 84 parasites per μ l in infected monkey blood and 61 parasites per μ l for *P. knowlesi* cultured in human blood. The *P. knowlesi*-specific FISH probe detected only *P. knowlesi* and not other species. The assay can be performed in 30 minutes, and could be a potentially useful tool for diagnosing *P. knowlesi* infections in remote laboratories in endemic countries (Shah J, et al; abstract 7321).

Among the future technologies, the development of microfluidic will allow the detection of multiple microorganisms at low cost [9]. One study reports the development and evaluation of a high throughput microfluidic system (Biospectrix™) that does not require culturing, identifies a broad range of bacteria in less than 1 hour directly from blood, and has a limit of detection of < 100 cfu/mL. After blood cells were lysed, bacteria were recovered in a filter and identified by FTIR (Krishnamurthy R, et al; abstract 6885).

Novel technologies, not growth dependent and based on flow cytometry have been developed for the rapid antimicrobial susceptibility testing directly from blood cultures. One of these commercialized methods is the FASTinov®. A study evaluated the performance of FASTinov® for susceptibility testing of *Pseudomonas aeruginosa* directly on positive blood cultures in 2 h. The overall categorical agreement between FASTinov® and broth microdilution was

95%. The highest categorical agreement was observed for gentamicin, ceftolozane-tazobactam and colistin (100%), followed by amikacin and imipenem (97% and 96%, respectively). The highest major error rate was detected for piperacillin-tazobactam, and the very major discrepancies were verified for meropenem (Costa-de-Oliveira S, et al; abstract 7343). Other platforms have also been developed for the rapid antimicrobial susceptibility testing. Among these, SeLux has developed an automated, rapid, low-cost, phenotypic AST platform that enables simultaneous, same-shift susceptibility testing full dilution series of a wide array of antibiotics. The core of this technology is an endpoint assay for bacterial surface area, which enables delineation of truly resistant bacteria from filamented or swelled organisms as can occur prior to lysis. In one study, AST was performed with the SeLux platform and compared against the Clinical and Laboratory Standards Institute (CLSI) broth microdilution reference method on a total of 1,100 bacterial isolates, including 300 "challenge" isolates, against 20 antibiotics. Susceptibility results with the SeLux platform were obtained within 5 hours from $> 90\%$ of the isolates tested. Essential and categorical agreement with the reference method were $\geq 90\%$ for all combinations tested. This platform constitutes an example of next generation phenotyping (Stern E, et al; abstract 5386). Among other new technologies presented at this meeting, the Acuitas® AMR Gene Panel u5.47 include the semi-quantitative molecular detection (real-time multiplex PCR) of 5 bacterial pathogens and 47 antibiotic resistance genes (including genes for aminoglycosides, cephalosporins, sulfonamides, fluoroquinolones, and trimethoprim/sulfamethoxazole) directly in urine specimens or bacterial isolates. The test identified urine pathogens with 96% semi-quantitative consistency compared with urine culture and accurately predicted phenotypic resistance for molecular results from urine with average accuracy from 82% to 94%. The molecular test can be used with statistical algorithms to predict phenotypic resistance to 17 antibiotics, providing results in 2.5 h (Walker G, et al; abstract 8969).

The implementation of the next generation sequencing (NGS) enables a fast microbiological diagnostic method without requiring a predefined range of suspicious pathogens [10]. One study, by using the BGISEQ-100 platform, evaluated the diagnostic efficacy of NGS in clinical samples from 1048 patients with suspected infections (234 blood stream infections, 284 respiratory infections, 312 central nervous system infections, and 218 focal infections). The overall NGS sensitivity was 46.5%, while blood stream, respiratory, focal, and central nervous system infection had a sensitivity of 78.72%, 89.4%, 96.4% and 19.4%, respectively, that was significantly higher than conventional laboratory methods (32.4%). The diagnostic sensitivity of protozoa and virus were the highest (100%), followed by virus (69.5%) and bacteria (74.29%), while fungi had a lowest sensitivity (33.3%). This study highlights the promising potential of NGS in the rapid etiological diagnosis of suspected infectious diseases (Ai JW, et al; abstract 8740). Other applications of NGS presented at

this meeting included the shotgun metagenomics for direct detection and identification of prosthetic joint pathogens in synovial fluid, the identification of organisms and resistance markers directly from urine specimens, and the detection of drug resistant tuberculosis directly from sputum samples, among others.

ANTIMICROBIAL RESISTANCE

Antimicrobial resistance remains a serious threat to public health worldwide, although resistance displays wide variations depending on the bacterial species, antimicrobial group and geographical region [11]. Development of antimicrobial resistance is caused by mutations in bacterial genes, or by acquisition of exogenous resistance genes carried by mobile genetic elements that can spread horizontally between bacteria. A series of plasmid-borne determinants conferring resistance to the last-resort antibiotics, carbapenems, aminoglycosides, and colistin have been described among different bacterial species. Since the first description in China in 2015 [12] of the transferable gene *mcr-1* conferring resistance to polymyxins, several studies have described the spread of *mcr-1* and other variants among *Enterobacteriaceae*. In one study presented at ASM Microbe, the authors describe for the first time the presence of a transferable chromosomally-encoded *mcr-5* gene in a colistin-resistant clinical isolate of *P. aeruginosa* in the USA. The isolate carried a chromosomal copy of *mcr-5* that was flanked by two copies of a novel Tn3-like transposon. The MIC of colistin was 16 mg/L (McGann P, et al; abstract 8054). Other study described the emergence of the colistin resistance gene *mcr-1* in four clinical isolates of *P. aeruginosa* in India, in which the gene was located on the chromosome (Pathak A, et al; abstract 4668).

Although resistance to carbapenems among *P. aeruginosa* isolates is, in general, chromosomally encoded, there is an increased emergence of plasmidic and transferable carbapenem resistance among this species. One study reported a novel carbapenem-hydrolyzing class D β -lactamase in a clinical isolate of *P. aeruginosa* in Korea. The carbapenemase was similar to OXA-10 (by the single substitution Lys103Asn), was located on the chromosome, and harbored by a new class 1 integron, suggesting the further spreading of this carbapenemase among Gram-negative bacteria (Park KS, et al; abstract 4338). Other authors reported the new carbapenemase NDM-11 among *E. coli* isolates in India. This carbapenemase is a variant of NDM-1 with a novel mutation at position 154 (Met to Val) and was located on a plasmid (Rahman M, et al; abstract 4322).

Ceftazidime-avibactam (CAZ-AVI) and ceftolozane-tazobactam (TOL-TAZ) are among the new antibiotics developed for the treatment of multi-drug resistant *P. aeruginosa*, however, isolates conferring resistance to both antimicrobials are described due to a variety of resistance mechanisms [13]. One study described the emergence of a high-risk ST309 *P. aeruginosa* clone harboring the carbapenemases GES-19 and GES-26, and conferring resistance to carbapenems, CAZ-AVI

and TOL-TAZ (Khan A, et al; abstract 6989). Two isolates of XDR *P. aeruginosa* isolates were recovered from patients at separate hospitals in Houston (USA), with a class 1 integron carrying multiple resistance determinants including GES-19 and GES-26. One patient cured with the combination of CAZ-AVI plus aztreonam.

Carbapenem-resistant bacteria are increasingly found in hospital settings, but little is known about their prevalence in the environment. One study reported the isolation and characterization of carbapenem-resistant bacteria isolated from samples collected from different public transit stations within the Los Angeles (USA) area. Among 25 samples collected from the validators and from the stations, a total of 34 meropenem-resistant isolates were recovered, and 21 of them were carbapenemase producers, indicating that public transit is an underappreciated reservoir of carbapenem-resistant bacteria (Carlson N, et al; abstract 4905).

NEW ANTIMICROBIAL AGENTS

In recent years, several new antimicrobials have been approved by the FDA [14] and some others are under development. One of the most interesting sessions of the congress was a plenary session dedicated to the description of early new antimicrobial agents [1]. Several new families of compounds with new mechanisms of action and active against multi-drug resistant Gram-negative bacteria were presented as follows: a) the odorhabdins, that inhibit bacterial translation with a novel mode of action on the ribosome; b) novel siderophore cephalosporins, like GT-1; c) inhibitors of LpxC, a zinc-dependent deacetylase responsible for the biosynthesis of lipid A, an essential component for Gram-negative bacteria; d) Mbx-4191, a pyranopyridine efflux pump Inhibitor in Gram-negative organisms; and e) VNRX-5133, a novel broad-spectrum β -lactamase inhibitor with selective direct inhibitory activity of both serine- and metallo- β -lactamases (MBLs). Moreover, new antimicrobials active against multi-drug resistant *Neisseria gonorrhoeae*, and antifungals active against *Candida auris*, with new mechanisms of action like APX001A, that inhibits Gwt1, an enzyme required for glycosylphosphatidylinositol post-translational modification of surface membrane-anchored proteins in fungi, were also presented. In addition, many poster presentations summarized the activity of other antimicrobials currently in phase 3 of development or recently included in the therapeutic arsenal. Among these, one study presented the activity of TOL-TAZ against *P. aeruginosa* from patients in different risk strata. Overall, the activity was >90% in all risk strata, and also maintained activity against 80% of the meropenem-non-susceptible isolates (Lob S, et al; abstract 4455). Other study presented the activity of CAZ-AVI against *P. aeruginosa* collected in Latin America from 2012 to 2016 (Wise M, et al; abstract 3492), and 92.6% of the isolates were susceptible, although a decrease in susceptibility was observed over the period of study due to the emergence of MBLs. A multicenter study evaluating the activity of

aztreonam-avibactam against *Enterobacteriaceae* and *P. aeruginosa* (Kazmierczak K, et al; abstract 3748) showed that this combination was active against 99.9% of Enterobacterales and against 100% of the MBL-producers. However, the combination showed reduced activity against all *P. aeruginosa* including MBL-positive isolates. Several studies evaluated the activity of imipenem-relebactam (IMI-REL) against multi-drug resistant Gram-negative organisms. In one of these, the overall susceptibility of *Enterobacteriaceae* to IMI-REL was 95.6%, and the activity was particularly high against KPC-positive isolates (98.5%) (Lob S, et al; abstract 4368). Meropenem-vaborbactam is another combination active against multi-drug resistant Gram-negative bacteria. One study that evaluated its activity against KPC-producing *Enterobacteriaceae* (Zhou M, et al; abstract 4966) showed that 97.6% of *K. pneumoniae* and 100% of *E. coli* were susceptible. Zidebactam is a β -lactam enhancer antibiotic (binding to PBP2a) that exhibits β -lactamase-independent, synergistic activity with other beta-lactams. In combination with cefepime shows potent activity against isolates resistant to meropenem, colistin, ceftazidime-avibactam and ceftolozane-tazobactam. In one study that included 1,018 carbapenem-resistant *Enterobacteriaceae* and 262 multi-drug resistant *P. aeruginosa*, >98% of the isolates were susceptible to this combination (Hackel M, et al; abstract 5397). Cefiderocol is a siderophore cephalosporin that has recently been introduced for the treatment of infections due multi-drug resistant organisms. In a worldwide multicenter study, the activity of cefiderocol was analysed against KPC-, NDM-, IMP-, OXA-48, and other OXA-producing isolates, and demonstrated potent *in vitro* activity against meropenem non-susceptible strains of *Enterobacteriaceae*, *A. baumannii* and *P. aeruginosa*, irrespective of the presence of serine- or metallo-type carbapenemases (Tsuji M, et al; abstract 3655). Tebipenem-pivoxil prodrug SPR994, is an oral carbapenem currently under development for the treatment of urinary tract infections. One study assessed the *in vitro* activity of SPR859, against a challenge set of *Enterobacteriaceae* including isolates with plasmid AmpC, ESBLs, KPC, MBLs and OXA-48-like enzymes. As expected, SPR859 showed potent activity only against isolates carrying ESBL and/or AmpC enzymes. These *in vitro* results indicate that SPR994 may be a candidate for stepdown therapy and empirical treatment where the prevalence of ESBL-producing isolates remains elevated (Mendes RE, et al; abstract 4603).

Concerning other non-beta-lactam antibiotics, eravacycline is a novel, fully-synthetic, fluorocycline that has completed phase 3 studies in complicated intra-abdominal infections and is in phase 3 development for complicated urinary tract infections. In a study that evaluated the activity of eravacycline against global isolates of *Enterobacteriaceae*, *Acinetobacter baumannii* (including carbapenem-resistant), *Stenotrophomonas maltophilia*, *Staphylococcus aureus* (including methicillin-resistant), and *Enterococcus* spp. (including multidrug-resistant isolates), the MIC_{50/90} for all *Enterobacteriaceae* (n=3157) was 0.25/1 mg/L, and for multi-drug-resistant-*Enterobacteriaceae* (n=666) was 0.5/2

mg/L. The MIC_{50/90s} for *Enterococcus* spp. and MRSA were 0.06/0.06 and 0.06/0.12 mg/L, respectively, and was also active against *A. baumannii* and *S. maltophilia* (Lawrence K, et al; abstract 5745).

Delafloxacin is a broad-spectrum fluoroquinolone active against Gram-negative (including *P. aeruginosa*) and Gram-positive (including MRSA) organisms that has been approved for the treatment of acute bacterial skin and skin structure infections and that is in clinical development for community-acquired bacterial pneumonia. One study evaluated the *in vitro* activity against a total of 3,629 *Streptococcus pneumoniae* clinical isolates from US and European hospitals including fluoroquinolone-resistant isolates (levofloxacin MIC >4 mg/L, or moxifloxacin MIC >2 mg/L). Delafloxacin demonstrated potent *in vitro* activity against all pneumococci (MIC_{50/90} 0.015/0.03 mg/L) and had excellent activity against all levofloxacin- and moxifloxacin-resistant isolates (Shortridge D, et al; abstract 4784).

Finally, among the new antifungals, rezafungin is a novel echinocandin as active as other echinocandins against common fungal organisms, but with distinctive pharmacokinetics that allow once-weekly dosing and high, front-loaded plasma drug exposure. In a phase 2 study, rezafungin was administered IV and dosed once weekly up to 4 weeks at either 400 mg (group 1) or 400 mg on week 1 and 200 mg thereafter (group 2) for the treatment of candidemia and/or invasive candidiasis. Rezafungin appeared to be safe and well-tolerated at both dosing regimens. The extended half-life and stability of rezafungin will be very useful especially in patients who could be discharged to outpatient therapy (Thompson GR, et al; abstract 7828).

Although antimicrobial resistance poses significant challenges for current clinical care, new classes of antibiotics are being developed, and new drugs hold promise against the challenge of multi-drug resistant bacteria.

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