ASM Microbe Annual Meeting – June 2019

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Sam Lam is a senior analyst and holds a Bachelor's degree in Biotechnology. Sam has 10 years of experience in competitive intelligence, syndicated analytics, drug forecasting, pharmaceutical regulatory procedures and medical writing. He has been associated with the Pipeline Intelligence team for 16 months.

The American Society for Microbiology (ASM) held its annual meeting on June 20-24, 2019 in San Francisco, USA where many infectious disease drug developers shared their data and outlined the path for the coming year. The ASM Microbe 2019 conference is the most comprehensive microbiology event and attracted more than 8,000 scientists and professionals from all fields of infectious disease prevention and treatment. The conference offered an opportunity for discussion, collaboration and advancement in drug development and infectious disease research. The meeting is designed to meet the needs of healthcare professionals, particularly physicians, clinical microbiologists, researchers and pharmacists specialising in infectious diseases with a focus on examining antibiotic resistance, new antibiotic development. The Pipeline Intelligence team attends the conference yearly to obtain the most up-to-date preclinical/clinical data presented by companies and information on the latest advances in microbiology sciences. This is a review of some of the most key data presented.

Combating carbapenem resistance

Infections caused by carbapenem-resistant Enterobacteriaceae are increasingly prevalent and are driven by the beta-lactamase enzymes carbapenemases, which degrade carbapenem antibiotics resulting in high levels of resistance and treatment failure. Carbapenemases are the main mechanism of resistance utilized by Gram-negative bacteria. Recently approved combinations of beta-lactam antibiotics with beta-lactamase inhibitors are active only against serine beta-lactamases-producing pathogens and there are currently no approved agents that specifically target metallo-beta-lactamases (MBL). Table 1 summarizes the key data presented for a selection of MBL inhibitors:

Company	Drug	Mode of Action	Data	Abstract Number
Antabio	**ANT 2681**	Thiazole-carboxylate MBL inhibitor	• In vitro antimicrobial activity against New Delhi metallo-beta-lactamase (NDM) producing Enterobacteriaceae clinical isolates • Potentiated carbapenem activity against strains carrying NDM variants, even under low pH conditions	P429 AAR-LB12
Qpex Biopharma	**QPX 7728**	Next generation beta-	• Potent inhibition of serine and class B metallo enzymes with no inhibition of mammalian serine and metallo proteases	P588 AAR-706

		lactamase inhibitor	• Restored activity of beta-lactam antibiotics against strains of Enterobacteriaceae, Acinetobacter baumanii and *Pseudomonas* aeruginosa producing beta-lactamases	
VenatoRX	**VNRX 5133**	Cyclic boronate-based serine and MBL inhibitor	• Potent in vitro activity in combination with cefepime against P. aeruginosa, including cefepime-, piperacillin-tazobactam- or meropenem-non-susceptible isolates	P588 AAR-722

Table 1

Other advancements in antibiotic development

Preclinical data were presented for Genentech's G 0775, an arylomycin analogue targeting the bacterial periplasmic signal peptidase LepB. Arylomycin is a recently discovered novel class of antibiotic that is active against Gram-negative bacterial infection. G 0775 demonstrated bactericidal activity against Klebsiella pneumoniae in a neutropenic thigh infection model and a neutropenic lung infection model. G 0775 also showed bactericidal activity against K. pneumoniae carbapenemase producing Escherichia Coli at low doses in a murine model of complicated urinary tract infection.

Researchers at the St Jude Children's Research Hospital, USA presented preclinical data for spectinamide 3408, a narrow-spectrum antitubercular agent. Spectinamides are semi-synthetic analogues of the antibiotic spectinomycin being developed for drug-resistant tuberculosis infections. At the target test dose of 400 mg/kg, administration of spectinamide 1810 and 3408 resulted in a significant reduction in lung burden in an acute Balb/c murine model. The antitubercular efficacy of both compounds were similar (1.13 and 1.11 log10 CFU reduction in the lung, respectively).

Researchers at Kitasato University, Japan reported preclinical data for nectriatide, a novel potentiator for the antifungal activity of amphotericin B against Candida albicans. Nectriatide, a 13-membered cyclotetrapeptide isolated from Nectriaceae species BF 0114, enhanced amphotericin B activity against Candida albicans, Saccharomyces cerevisiae and Rhizopus oryzae. The reduction in MIC values of amphotericin B in combination with nectriatide (32 mcg/mL) against C. albicans, S. cerevisiae and R. oryzae were 0.031, 0.031 and 0.25 mcg/mL, yielding a 16-, 16- and 4- fold potentiation in activity, respectively.

Summary

Antimicrobial resistance is rising and has become a major threat to global public health and food safety as well as an economic burden. The high prevalence of Gram-negative bacterial resistance, particularly with the emergence of meticillin-resistant Staphylococcus aureus, resistant *P. aeruginosa* and superbug NDM 1 positive Enterobacteriaceae, have compromised the most effective treatments. Further elucidation of resistance mechanisms and greater innovation in the development of new antibiotics coupled with new effective control strategies are vital in combating antimicrobial resistance.