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EDITORIAL

Blue sky and some shadows: new antibiotics and new superbugs

The ECCMID 2016 in Amsterdam

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What is the latest news in infectious diseases and clinical microbiology? This question is so important for about 11,000 physicians, researchers, developers and also for the diagnostic and pharmaceutical industry from almost all countries on this planet that they travel to the place where they can see it all at once: about 3000 scientific contributions in oral presentations, posters and e-posters. For many, the focuses of interest were two topics: the spread of resistant organisms including what can be done against it and the development of new antibacterials.

The single most important focus was the emergence and possible spread of gram-negative bacteria expressing the MCR-1 gene, a gene that confers resistance against colistin [1]. On the one hand, this antibiotic still serves as a sort of last-line antibiotic against mdr (multi drug resistant) bacteria; on the other hand the occurrence of MCR-1 is associated with the horizontal transfer of additional mechanisms via plasmids [2]. The fact that colistin is much more often used in animal production than in humans shed light on the everlasting question how can we coordinate political action that confines antibiotic use in animal farming. In addition to news on MCR-1, many other contributions at the conference reported on the spread of metallo-betalactamases, carbapenemases and resistance genes in gram-positive bacteria. Not all contributions saw the "battle lost"—several intelligent an enthusiastic infection control colleagues invited to concerted action on all fronts of the struggle against resistant bacteria and their travel from individual to individual, from country to country and from continent to continent. We might confine the spread and in several contributions at the conference examples of interventions were shown that really had the effect of less nosocomial transmission and a reduction of prevalence of mdr [3]. This could be called the good weather fraction of researchers and really: the first 3 days April 9 through 11 there was blue sky and sun in Amsterdam.

Additional interesting tracks of the scientific program were the development of new antibacterials and presentations of pre-clinical and clinical data on new antibiotics and new target structures. Antibiotics already in clinical development phases were presented by Winfried Kern (Freiburg) in an oral presentation with a focus on tetracycline-derivatives and quinolones [4]. New compounds in this field are eravacycline and omadacycline. Both are being evaluated for complicated intra-abdominal infections. While eravacycline's phase III trial results had already been presented last year [5] at the ECCMID, omadacyclin seems also to be of use in skin and skin structure infections (comparative trial with linezolid) and it shows activity against *Clostridium difficile*. Both, intravenous and oral administration can be used at doses of 100 mg i.v. and 200–300 mg by mouth. Both antibacterials show some similarities with tigecycline, an antibiotic that still has its role the treatment of infections due to mdr [6].

While there was no new licensure of a quinolone for a long time, now several compounds are in development, for example delafloxacin, nemonoxacin, avarofloxacin and finafloxacin. The interesting point about delafloxacin is that it is not zwitterionic and is said to become active at lower pH, e.g. as present in inflamed tissue. Enhanced intracellular activity is also an interesting feature. Some of the other quinolones referenced by Kern are being tested for skin infections, respiratory infections and some seem also promising

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against gonococcal disease, which may be good news in times of ever growing resistance against cephalosporins in gonococci. And this indication is also being tested with solithromycin, another tetracycline-derivative quoted by Ursula Theuretzbacher (Vienna) in her enthusiastic talk on new pipeline antibacterials. Compounds with new bacterial target sites were also included, like pleuromutlin, defensin mimetic antibacterials, Fab-I inhibitors (inhibit bacterial fatty acid synthase II pathway), pdf inhibitors and type 2 topoisomerase inhibitors. Moreover, several new betalactamase-inhibitors in different stages of development for preclinical to clinical phase were listed and that is also good news in the combat against mdr organisms. But there is also a new compound in the long row of aminoglycosides: plazomicin, a novel compound that seems optimized to overcome cross resistance against aminoglycosides.

A completely different approach is the development of vaccines and monoclonals against bacterial toxins. Several developments in this direction include VLA43, an anti-*Pseudomonas aeruginosa* vaccine in phase II and III development, a *C. difficile* monoclonal bezlotoxumab that neutralizes the effects of toxin A and toxin B. Moreover, an anti-staphylococcal compound MEDI4893 against alpha-toxin of *Staphylococcus aureus*.

New concepts in pre-clinical development, finally, were presented on April 12 in a morning session. For example: a VanR inhibitor with the potential to resenstitize vancomycin-resistant enterococci towards glycopeptides. This is being achieved in vitro by a newly developed "transcription regulator inhibitory compound" (TRIC) which seems to be able to switch off the expression of the glycopeptide resistance trait of enterococci (Michel Pieren, Basel). Another concept is the inhibition of LpxC by an inhibitor PF-5081090 which augments susceptibility to rifampin, azithromycin, vancomycin in *Acinetobacter baumannii* by a loss of lipid A resulting in an increase of membrane permeability (Meritxell Garcia-Qunitanilla, Sevilla). Eileen Rubio (Cambridge, MA, USA) presented data on an MvfR inhibitor (multiple virulence factor regulator) SSPR00305 in Pseudomonas. The inhibition of this global transcription regulator resulted in clinical success in several animal infection models with resistant *Pseudomonas* strains. Another talk was on Apidaecin, Api137, which is highly efficient against susceptible and resistant *Escherichia coli* and *Klebsiella pneumoniae* in murine intramuscular thigh and ascending urinary tract infections. The mode of action seems to be the inhibition of the ribosome-assembly (Daniel Knappe, Leipzig). Last, but not least there were contributions on antimicrobial peptides (AMPs), one of which is antimicrobial peptide M33 presented by Hessel van der Weide (Rotterdam): the time kill kinetics against *Klebsiella* strains and other gram-negatives were shown to have highly effective activity which is concentration dependent and shows activity in strains resistant against colistin.

This might close the circle of our quick ride through ECCMID: from colistin resistance to new compounds against it and we may look forward to a new exciting year in infectious disease research. Infection will continue to contribute with up-to date contributions.

Compliance with ethical standards

Conflict of interest None.

References

1. Liu YY, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. Lancet Infect Dis. 2016;16:161–8.
2. Zurfuh K, et al. Occurrence of the plasmid-borne mcr-1 colistin resistance gene in extended-spectrum-beta-lactamase-producing Enterobacteriaceae in river water and imported vegetable samples in Switzerland. Antimicrob Agents Chemother. 2016;60:2594–5.
3. Jung N, Lehmann C, Fatkenheuer G The "choosing wisely": initiative in infectious diseases. Infection. 2015.
4. Kern WV. New antibacterial agents on the market and in the pipeline. Internist (Berl). 2015;56:1255–63.
5. Draenert R, et al. Novel antibiotics: are we still in the pre-post-antibiotic era? Infection. 2015;43:145–51.
6. Heizmann WR, et al. Clinical efficacy of tigecycline used as monotherapy or in combination regimens for complicated infections with documented involvement of multiresistant bacteria. Infection. 2015;43:37–43.