monoclonal antibody), or screening for latent TB before using TNF inhibitors.

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Type: Invited Presentation

Final Abstract Number: 30.004
Session: Infections in the Era of Cancer Treatments, Transplants and New Biologics
Date: Saturday, March 5, 2016
Time: 10:15-12:15
Room: Hall 1

Cytomegalovirus

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Abstract: Cytomegalovirus (CMV) remains an important pathogen in transplant patients. Sensitive and rapid turnaround quantitative PCR based monitoring coupled with the availability of effective antiviral therapy has reduced the overall burden of CMV disease after transplantation. However, in hematopoietic stem cell transplant (HSCT) patients, the increasing use of new donor and stem cell sources present new challenges in the prevention and treatment of CMV. Gastrointestinal disease is now the most common end-organ manifestation of CMV infection after HSCT, whereas pneumonia remains associated with high mortality. In addition, indirect effects of CMV infection continue to have both positive and negative effects on outcomes after HSCT. Antivirals with novel mechanisms of action and improved toxicity profiles compared to those currently available are in late phase clinical trials. Also CMV vaccines are in development. Despite these advances, CMV is likely to remain a significant pathogen in transplant recipients.

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Final Abstract Number: 31.001
Session: New and Recently Approved Antibiotics: Challenges and Opportunities
Date: Saturday, March 5, 2016
Time: 10:15-12:15
Room: Hall 2

New antibiotics: What do we need?

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Abstract: Lack of effective antimicrobial therapy for multidrug-resistant organisms (MDROs) has been a growing concern particularly due to spread of extended-spectrum beta lactamase (ESBL) and carbapenem resistant *Enteriobacteriaceae* (CRE). Better therapeutics for MDROs are needed.

Common MDROs include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococcus (VRE), ESBL and CRE. Gram-positive organisms such as MRSA and VRE are stable or declining in frequency while gram-negative ESBLs and CREs are increasing. Recent antibiotics generally focus on MRSA and gram-positive MDROs with few new agents effective against gram-negative organisms. Outside of common healthcare-associated MDROs, Gonococcus has become highly antibiotic-resistant in many parts of the world. Furthermore, most therapy for MDROs is intravenous and associated with a high rate of adverse effects and burden of disease related to long courses of treatment.

New antibiotics are needed with novel mechanisms of action against MDRO organisms, fewer side effects, less impact on the microbiome and easier, non intravenous delivery. Studies of new drugs need to focus on rational use with minimal duration, easiest form of delivery and clear recognition of effects on the microbiome. Use of new antibiotics must be appropriate and avoid overuse. Choosing Wisely and the growth of Antimicrobial Stewardship may help appropriate use.

Finally, a new model of infectious disease management is developing based around the microbiome. Manipulation of the microbiome may become a mainstay for treatment of many diseases. Currently, fecal transplants for C. difficile are the only approach to microbiome manipulation proven to work. Other uses may include decolonization of MDROs from the gastrointestinal track. Future microbiome manipulations may include targeted microbiome changes via capsules to the GI tract and possible inoculations to the skin or mucosal surfaces. Development of ways to manipulate the microbiome could improve treatment of infectious disease without producing antibiotic resistance.

Development of antimicrobials active against ESBLs, and CRES that are safe and easy to use is needed. Longer range antimicrobial therapies will likely involve microbiome manipulation.

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Room: Hall 2

The antibiotic pipeline: What can we expect?

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Abstract: Antibiotic resistance is widespread. Despite the recognized and growing need for new antibiotics, today most large pharmaceutical companies have dropped active antibacterial drug discovery programmes. While antibiotics are regarded as non-profitable compared to other fields, small companies—mostly backed by promising academic discoveries—are stepping in to drive research and early clinical development in the antibiotics field. In the 1980s and 90s the antibiotic pipelines were satisfying the need for improved antibiotics against the prevalent resistant strains at that time. Currently, extensively- or pan-resistant Gram-negative bacteria require novel antibiotics without co- and cross-resistance to known drug classes. A few research&development programs based on classical antibacterial compounds against Gram-negative bacteria that bind to new targets or have a new mode of action are in the early research phase and their potential is difficult to assess. Due to such thin discovery pipelines, attitudes have changed and antibacterial approaches outside the mainstream are increasingly pursued and publicly funded. These alternative methodologies range from peptides and peptidomimetics to antibodies, prophylactic and therapeutic vaccines, adjunctive

therapies, bacteriophage cocktails. The value of such approaches as well as the regulatory pathways are not clear yet. Potentiating strategies have seen a resurgence in recent years and are focused on blocking specific resistance mechanisms such as beta-lactamases, resistance-regulating determinants, preventing transfer of resistance plasmids or on protecting the microbiome, disrupting biofilms, targeting dormant bacteria, blocking virulence factors, or supporting the immune system. In response to relaxed regulatory requirements and economic incentives, recent years have seen a trend towards reviving old drugs (e.g. fosfomycin, fusidic acid, minocycline, aztreonam), modifying old drugs (e.g. colistin) or potentiating old drugs (e.g. combination of approved drugs, ß-lactamase-inhibitor combinations). These approaches will not solve our major problems with resistant bacteria but may buy some time.

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Room: Hall 2

Incentivizing antibiotic innovation

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Abstract: Antibiotic resistance can develop quickly. The CDC demonstrated in 2013 that the first reported cases of bacterial resistance occurred in less than three years after market introduction of six key antibiotics. Yet antibiotic innovation is progressing at a more sedate pace, with only seven new classes of antibiotics launched between 2000 and 2014 (Laxminarayan 2014). One reason for this mismatch is that the pharmaceutical industry is not incentivized to develop new antibiotics. Existing, generic antibiotics are inexpensive and still generally effective. New classes of antibiotics are often necessary for only a small number of patients or as an insurance mechanism for potential future outbreaks, making the return on the sizeable investments in research and development insignificant or negative. These poor returns encourage the pharmaceutical industry to focus their efforts elsewhere. Yet resistance continues to emerge, and if we wait until a major outbreak occurs, given the long lead-times for developing a new antibiotic, it will be too late. New incentives are necessary to stimulate greater antibiotic innovation, and they must be linked to the sustainable and appropriate use of the resulting antibiotic. Otherwise resistance may develop faster. New incentives need to reward developers for their knowledge generation, not the number of treatments sold. They also need to ensure that patients receive the necessary antibiotic, regardless of income status. These are fundamental changes to the current reward system for pharmaceutical innovation. The EU-financed Innovative Medicines Initiative project, Driving reinvestment in R&D for antibiotics and advocating their responsible use (DRIVE-AB), is tasked with identifying new, sustainable economic models as well as recommendations for a viable path forward to greater antibiotic innovation.

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Basic improvement methods in stewardship

A.H. Holmes

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Abstract: Pragmatic strategies to improve antibiotic prescribing will be discussed in this session. Although a whole healthcare economy approach to antibiotic stewardship will be advocated, the particular focus will be within acute health care. Implementation and adoption will be considered along with improvement methods in stewardship. Supporting organisational models will also be reviewed and practical examples and case studiesdescribed. The real and potential challenges faced in delivering effective antibiotic stewardship and sustaining improvement will be discussed.

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Room: Hall 5

Update on HIV Prevention

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Abstract: In recent years, definitive studies have demonstrated the effiacy of the use of antiretroviral medications for primary and secondary HIV prevention. The HPTN 052 trial enrolled 1,752 partners in HIV discordant couples in Africa, Asia and the Americas, and randomized the infected partner to receive immediate versus deferred antiretroviral therapy. HIV-infected participants who immediately initiated treatment were more than 96% less likely to transmit HIV to their partners compared to those in the delayed arm. The public health benefit of early treatment has been corroborated by population level studies correlating decreasing HIV incidence in several areas of southern Africa with access to early initiation of antiretrovirals. However, since the majority of people living with HIV globally are unaware of their infection, and less than 1/3 are virologically suppressed, new approaches to primary prevention for high risk seronegatives are also needed. Ten randomized, controlled trials of antiretroviral pre-exposure prophylaxis (PrEP) have been conducted, with studies in men who have sex with men, heterosexual discordant couples, and injection drug users finding that oral tenofovir-based regimens have been effective in decreasing HIV incidence. Several studies of PrEP in young African women have not demonstrated efficacy, while others have, with variable levels of medication adherence explaining most