54th ICAAC, Washington DC conference – selective innovation won’t do!

LONDON, UK----10TH September 2014----ExpertREACT. Advances in new HIV and HCV antivirals prove that we can make rapid progress in novel anti-infectives. However, it seems that economics rather medical need has too much influence on our focus and motivation.

Our continual battle against the infectious micro-organism and its propensity to cause human disease and suffering is fought on the two main fronts of treatment and prevention. Recently, worldwide delegates convened in Washington, DC at the 54th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) conference to discuss advancements in both areas. VacZine Analytics was in attendance and in this ExpertREACT article will discuss the main themes of the conference and our perspective of their significance.

Aside from Ebola, small molecule therapeutic management of infections, both bacterial and viral, dominated sessions at the conference. This was not surprising since new drugs have been recently approved including four new antibiotics for the US market. These antibiotics: Orbactiv™ (Oritavancin), Sivextro™ (tedizolid), Teflaro™ (Ceftaroline) and Dalvance™ (Dalbavancin), although bringing some excitement to an otherwise inactive field, are not new classes of drugs and mostly have a Gram positive rather than the much needed Gram negative bias. However, their emergence reignited the debate at the Keynote address given by John Rex (AstraZeneca) about whether the industry is suitably incentivized to continue research into finding novel antibacterial agents given that the economics is challenging when compared to other fields.

Antibiotics are clearly of “great value to society”, far beyond the dollar revenues to be gained by a manufacturer, but unless stakeholders find new ways to compensate industry, alongside advocating a paradigm of restricting use due resistance development, innovation will suffer. Clearly a paradox – and exemplified by the fact that all of the four new antibiotics are being marketed by smaller or at best, mid tier players such as Cubist, Forest Pharmaceuticals, the lesser known Medicines Company and Duranta. Cubist, stand out and should be applauded making impressive progress & commitment to the field of antibiotics now having three marketed products: Sivextro™, Daptomycin (Cubicin™) and Dificid™ (Fidoxamicin). They gained Dificid™ by the ~$550m acquisition of Optimer Pharmaceuticals back in October 2013 (1). Clearly, the days of the antibiotic giants such as GSK, Pfizer and Johnson and Johnson have passed as their once dominant blockbuster products have now been eroded by generic forms.

One speaker mentioned at ICAAC, “why can’t antibiotics cost the ~$75K to save a life similar to novel cancer and antiviral therapies?” Comments to this effect mostly explain why the large manufacturers have reduced their antibiotic development focus. Commercially, the development of antiviral agents with longer therapy durations and higher pricing thresholds continue to spur advancements in both HIV and now, HCV. HIV can now be managed with highly novel integrase inhibitors, the newest of which is ViiV Healthcare’s Tivicay (dolutegravir), which according to one speaker, almost has “wonderdrug” like status due to its apparently huge barrier to genetic resistance since launch in 2013. Dolutegravir can now also be administered as a fixed dose combination along with abacavir and lamivudine in the recently approved Triumeq product (2). Things have indeed come a long way since zidovidine (AZT) monotherapy back in 1987.

Similarly, in HCV, new directly acting antivirals such as the NS3-4A protease inhibitors telaprevir (Incivek®) /boceprevir (Victrelis®) and sofosbuvir (Solvadi®), the NS5B RNA-dependent RNA polymerase inhibitor have revolutionized therapy which once relied on harsh regimes containing only pegylated interferon and ribavirin. Even the highly critical UK NICE committee has provisionally approved Solvadi for use at ten or thousands of pounds per patient due to its avoidance of highly expensive downstream complications which can involve liver transplantation (3). The key question is therefore: what advances could have been made in antibiotics if the economics were as attractive as antivirals? Would our inherent fear of multidrug resistant bacteria species such as carbapenem resistant enterobacteriaceae (CRE) which currently kills hundreds in the US each year (4) be lifted? It simply does not make any sense that a death from a bacterium should be worth less to us than that from a virus.

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We shall await the outcome of initiatives covered by Dr Rex and presented at ICAAC which aim to address this ideological flaw and spur development of new antibiotics.

Vaccines were not centre stage at the 54th ICAAC with three of the largest manufacturers, GSK, Pfizer and Sanofi Pasteur not even having exhibitor stands. However, there were still some important discussions especially around latest disease dynamics and the impact of vaccination. One notable topic was the re-emergence of pertussis discussed in countries such as the US, UK, Argentina and Mexico. For Argentina, cases increased 90% in 2012 with most deaths <1 yrs (before primary immunization can be completed). Similarly in the US, Health Care Utilization Project (HCUP) data were presented showing an estimated 44% (n=9,500) of pertussis-associated emergency department visits (2006-11) occurred among infants less than one year of age (4). The resurgence of neonatal pertussis has prompted widespread maternal vaccination programs which have been successful in reducing mortality. The UK program which began Oct 2012 with combined low dose diphtheria, acellular pertussis, and inactivated poliomyelitis vaccine (Repavax) was reported at ICAAC to have given no safety issues despite a large cohort of women being vaccinated in their 3rd trimester (5). Such programs are giving policy makers including WHO SAGE more confidence in maternal immunization strategies possibly also for the developing world although questions around the use of whole cell pertussis will remain.

Other potential maternal vaccine strategies for RSV (Novavax) and CMV (VBI vaccines) were also discussed at ICAAC. Novavax presented data showing that their F-glycoprotein RSV vaccine when given to pregnant mothers could protect infant baboons when challenged with RSV in a manner comparable to palivizumab therapy (6) indicating preclinical proof of concept for its Phase II candidate. Second only to malaria, RSV was cited to kill more infants than any other global pathogen. A vaccine is greatly needed but is there the required level of urgency? One industry executive complained to VacZine Analytics that in the US, it’s been 2 years since series A funding was granted to a biotech focused solely on prophylactic vaccination. Even in 2011 the sum was only $11m compared to $100m in non vaccine areas (7).

Yes – we are making more progress with new vaccines e.g. meningococcal serogroup B and now, dengue; but given the immense power of vaccines to save lives and alleviate suffering, in common with novel antibiotics, we are not doing enough.

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Top 5 companies: GSK Biologicals, Sanofi Pasteur, Merck & Co, Pfizer (Wyeth) and Novartis Vaccines and Diagnostics

References and Notes:


7) Personal communication. CEO undisclosed company.

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