Meningococcal group B vaccine, Bexsero®: too late for the science? Stick to the wider economics.

LONDON, UK----11th November 2013----ExpertREACT. Retrospective analysis of the UK success of *meningococcal* group C vaccine has scientifically set the bar too high for the group B vaccine, Bexsero®. Pushing forward consideration of the wider economic case is the best chance for Novartis & MRF

Once again members of the healthcare community met recently in London to attend the Meningitis Research Foundation (MRF) meeting, Meningitis and Septicaemia in Children and Adults 2013. This year the meeting had a unique backdrop in that a preventative vaccine against *meningococcal* group B had been recently licensed in the EU (4CmenB, Novartis' Bexsero®) but was unyet recommended for inclusion to the UK national immunisation programme (NIP). Unsurprisingly, the recent interim statement by the UK Joint Committee on Vaccination and Immunisation (JCVI) decided June 12, 2013 **(1),** dominated most of the discussion at the MRF meeting with the viewpoints put forward by those in support and those against the groundbreaking decision. This **ExpertREACT** article will summarize some of the main points brought up in the meeting.

Back in the summer the JCVI concluded that based on the available evidence at that time Bexsero® was unlikely to be cost-effective for infant and toddler immunisation *"at any vaccine price based on the accepted threshold for cost effectiveness used in the UK."* This decision was of great disappointment to members of the MRF which include researchers, healthcare stakeholders and above all, families that have been affected by the severe impact of *meningococcal* group B infection. The news was also a significant setback to loss-making Novartis Vaccines division which had so far invested 17 years of research into the vaccine and was relying on the UK recommendation to begin recouping its financial investment. Previously with *meningococcal* C vaccination in the late 90s the UK set a global precedent in successfully tackling the disease, allowing other countries to follow suit. It was hoped that the U.K.'s potential "early adopter" status for Bexsero® would initiate another cascade for sequential country introduction.

The basis of the JCVI interim statement decision is centred around an independent cost-effectiveness model which currently has not been made public, but formulated by the same University of Bristol and the London School of Hygiene and Tropical Medicine partnership which previously published a similar version. The published version concluded that new menB vaccines could be cost-effective *"if competitively priced, particularly if the vaccines can prevent carriage as well as disease"* **(2)**. Therefore there was much discussion at the meeting regarding the potential differences between these models and most of all the model input parameters used and their reliability.

The most critical inputs to the cost effectiveness model are variable and are centred around the three main areas of 1) Disease burden 2) Vaccine strain coverage/effectiveness and 3) Vaccine impact on carriage. In terms of disease burden, while *meningococcal* outbreaks can occur and overall incidence follows an unpredictable natural fluctuation, a key negative factor taken up by the JCVI committee is that although *meningococcal* group B remains the predominant serotype in the UK (~87% of cases), and mainly occurs in children below 2 yrs, the actual burden of B disease has reduced by almost half since late 90s. For example, in the 1998/99 epidemiological year for England and Wales there were 1,400 cases of group B disease out of a total of 2,773 (all sero types) , whereas in 2011/2012 there were 614 cases out of a total of 766 **(3)**. Therefore, from the societal perspective, the question does arise: is it a worthwhile exercise to vaccinate ~730,000 infants born each year to prevent <1000 cases of group B disease assuming the vaccine is highly effective.

Until the menB vaccine is actually deployed in a real use setting with subsequent post marketing surveillance it is difficult to tell how effective it will be. Novartis have used a system known as Meningococcal Antigen Typing System (MATS), which predicts the vaccine may be effective against 73% of UK Men B strains and are hoping that new data suggesting MATS underestimates coverage impacts future decision-making. A recent publication suggests coverage could be as high as 88% **(4)**. Novartis also state any potential cross protective effect against other men serotypes is not taken into account for their vaccine.

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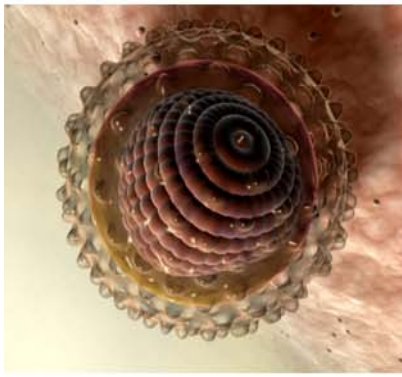

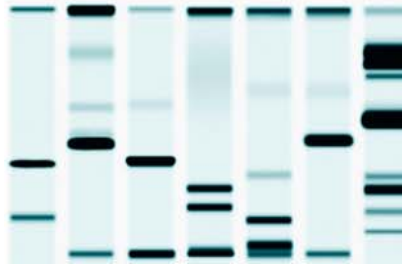

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It is now known that other vaccines such as Hib, *pneumococcal* and *meningococcal* C have exerted their huge effects on public health by virtue of their ability not only to provide direct antibody protection, but to impact upon nasopharyngeal carriage and generate "herd" immunity. Indeed, data cited at the meeting indicates that the group C vaccine generated an 81% reduction in carriage for 15-19 yrs, which in turn generated a 67% reduction in unvaccinated cohorts. It is this "free" impact of the vaccine that the JCVI would consider highly desirable for Bexsero®. To this end Novartis have conducted an investigator initiated study in 2968 university students, but found while 2 doses of Bexsero® elicited strong immune responses no clear association between carriage rates and hSBA levels were identified **(5).** While a subgroup analysis has shown some effect on the acquisition of carriage in high risk groups, including smokers it is clear that Bexsero® has some way to go into achieving this claim.

The model parameters of disease burden, vaccine coverage and impact on carriage discussed above in a sense are governed by rational scientific data and could be viewed more rigid than some of the economic inputs to the model which attempt to capture the cost of illness related to serogroup B disease. Many at the recent MRF meeting were of the view that the current cost effectiveness model used by the JCVI is too simplistic in that it does not quantify the wider impacts of the disease, i.e. impacts on other family members, carers and health care system as a whole. A case of serogroup B disease is estimated to account for millions of pounds of spending over an affected child's lifetime, especially in severe cases of the disease. The Meningitis Research Foundation (MRF) has recently submitted a detailed response to the JCVI encompassing all economic arguments with supporting data **(6).** A notable point is whether other currently used life saving vaccines (HPV and rotavirus) would have been introduced using the JCVI methodology. Thankfully, a recent development is that the JCVI have agreed to reconsider the inputs to their cost effectiveness model.

Looking at the story so far, it appears that strengthening the economic arguments around Bexsero® are the best chance Novartis has for its introduction. It seems retrospective analysis of the success of *meningococcal* group C vaccination has set the scientific "bar" too high for group B. Seemingly the regulators want the same thing for a different vaccine.

References and Notes:

1) UK Joint Committee on Vaccination and Immunisation (JCVI). Meeting minutes. Available at: https://www.gov.uk/government/policy-advisory-groups/joint-committee-on-vaccination-and-immunisation#minutes. Accessed November 2013

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6) Meningitis Research Foundation (MRF). OUR RESPONSE TO THE JCVI. Ninth of September 2013. Available at: http://www.meningitis.org/news-media/our-response-to-the-jcvi-72756. Accessed November 2013