GSK's Rotarix: how to differentiate?

LONDON, UK----25 February 2008----ExpertREACT. GSK Biologicals recently announced that the US regulatory authorities (VRBPAC) have recommended its new human rotavirus vaccine, Rotarix for US approval. The FDA action date for the Rotarix biologics license application is April 3. Along with the recently submitted *pnuemococcal* vaccine Synflorix (EU), GSK could now have two key vaccines aimed at dislodging incumbent rival products: Prevnar (Wyeth) and Rotateq (Merck & Co). With the US approval of Cervarix uncertain, GSK will need to work hard on communicating the "right" added benefits of its new products.

Rotavirus is the most common cause of severe gastroenteritis in infants and young children (< 5yrs) worldwide. The virus is spread by the fecal-oral route and causes around 650 – 700,000 deaths annually, 80% of which occur in underdeveloped regions (1). Rotavirus hospitalizations are most common from 7 to 15 months after maternal antibodies to the virus have waned, however a significant burden of disease can occur earlier. For example, it is estimated that between 5-10% of rotavirus diarrhea can occur before 3 months of age and 20% before 6 months of age necessitating earlier protection.

Rotavirus infection is often refered to as a "democratic" disease because most children, whether from rich or poor families, have contracted the virus by the age of five. Although the impact in terms of rotavirus related deaths is much lower in the West, the virus still is responsible for ~400,000 US physician visits and 50-70,000 US hospitalizations due to dehydration. Direct and indirect costs of the virus are estimated at a significant >$1 billion per year making preventation vaccination a cost effective strategy (2).

Rotavirus vaccines mimic the natural immune response to the virus and are designed to cover the majority of circulating virus strains that cause diarrhea. Rotavirus has 5 key serotypes which can change yearly and differ by geography: G1P [8], G2P [4], G3P [8], G4P [8] and G9. The G9 strain, covered by Rotarix but not Rotateq has recently emerged becoming common in Asia and Latin America.

Because rotavirus is considered a significant problem, the US FDA previously approved the first rotavirus vaccine as long ago as 1997. US-based Wyeth launched the rhesus-human reassortant vaccine, Rotashield in 1998. Unfortunately the vaccine was withdrawn after 9 months and ~600,000 vaccinations due to a temporal rare association with intussusception of the bowel (15 observed cases). Intussusception is very rare but can be fatal if not treated. It was found to occur mostly in children 5 to 10 months and during a 3 –14 day period after the first dose of the vaccine.

The experience with Rotashield has forced new rotavirus vaccine manufacturers to work hard in allaying any concerns with their newer vaccines. Both executed huge clinical development plans and have significant "real use" experience around the world. GSK for example, state that the US submission of Rotarix will include data from nearly 75,000 infants (3). Rotateq, which is a human-bovine vaccine, has already been US approved since 2006. No significant safety concerns with either product have been reported so far.

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If Rotarix gains a US license many observers will be following its future progress against Merck & Co's Rotateq, which sold an impressive $586m in 2007. Merck & Co estimate that their product has penetrated 60% of the US birth cohort and will maintain the number one position (4). However, now with a positive comment from VRBPAC, GSK will now be gearing up for an aggressive US launch.

VacZine Analytics believes that the real question will be around which differentiator will GSK choose for their product? There are potentially many and the ability to focus will be critical to success. For example, Rotarix is a 2-dose vaccine rather than 3 allowing vaccine completion by four months of age, it offers coverage against serotype G9 and it is based on human strains only. While some of these potential differentiators are stronger and more rational than others it is likely that the shorter schedule will hold the most resonance with decision makers. On balance it is of note that the US committee did not vote on GSK's data for serotype G2 and were also concerned about an increased tendency of pneumonia and convulsion-related serious adverse events in vaccinated subjects.

Regardless of which strategy GSK selects for the US market, the global peak market for rotavirus vaccines is estimated at close to $3 billion. Through the rotavirus vaccine program (RVP) additional GAVI funding mechanisms have also been discussed for the predicted 160 million-dose demand in developing countries (5). Although there are some mid stage competitor vaccines being tested in India and China it would appear both Rotarix and Rotateq will dominate the global stage in many years to come.

References:

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VacZine Analytics is a new strategic research agency based in the United Kingdom. Its aim is to provide disease and commercial analysis for the vaccine industry and help build the case for developing new vaccines.