Novartis Vaccines: all guns blazing on meningitis.

LONDON, UK----22 May 2008----ExpertREACT. Recently, Novartis Vaccines announced encouraging new data for its investigational meningococcal group B (MenB) vaccine (1). MenB remains the only major disease-associated serogroup for which there is currently no licensed vaccine available in the US or European markets. With a significant head start on its competitors, a Phase IIII MenACWY program and experience in MenC, Novartis could dominate future meningitis vaccination.

Neisseria meningitidis is a common cause of meningitis and sepsis in children and adults that can result in brain damage, blindness, deafness and death. Five major serogroups of *N. meningitidis* (ACWY & B) are responsible for most meningococcal diseases worldwide. Effective vaccines for serogroups ACWY are available, which include Menactra (Sanofi Pasteur), the only tetravalent conjugated ACWY vaccine approved in US, and Menjugate (Novartis Vaccines) and NeisVac-C (Baxter) which have successfully controlled serogroup C disease in Europe. Meningococcal group B (MenB) remains the only major disease-associated serogroup for which there is currently no licensed vaccine available in the US or European markets, although Novartis Vaccines (formerly Chiron) developed MenZB for a specific MenB strain prevalent in New Zealand.

MenB infections are considered to be the most lethal form of meningococcal disease, responsible for around 30% (2) and from 40% to 90% (3) of infections reported in the US and Europe respectively. MenB causes a disproportionately large number of cases among infants, accounting for around 50% of infections in children under the age of five in Europe (4). A major hurdle in the development of a MenB vaccine has been the diverse and changing sub-strains of the serogroup. Also MenB differs from ACWY serogroups because it has a capsular polysaccharide which also present in many human glycoproteins. Therefore polysaccharide–protein conjugate vaccine approaches may induce vaccine hyper-responsiveness. Novartis Vaccines have circumvented these challenges by producing a recombinant vaccine which contains three protein antigens identified through reverse vaccinology techniques. These are coupled in the candidate formulation with Men B outer membrane vesicles (OMV) (4).

New Phase II data for Novartis MenB vaccine were presented at the European Society for Paediatric Infectious Diseases (ESPID) annual meeting in Graz, Austria on May 14, 2008.The vaccine was administered concomitantly with routine immunizations at 2, 4 and 6 months of age, along with a booster dose at 12 months of age. Infants were randomized to receive either the MenB vaccine with an outer membrane vesicle (OMV) from *N. meningitidis* strain NZ98/254 or MenB proteins alone. Antibody levels were measured by serum bactericidal assay using human complement (hSBA) and a test panel of three MenB strains (44/76-SL, NZ98/254, 5/99) representing >70% of the MenB disease burden in the US and EU. The vaccine was most effective when combined with OMV-NZ98: the proportion of infants with antibody titres >1:4 after the third dose were 89% for the 44-76/SL strain, 96% for the 5/99 strain, and 85% for the NZ98/254 strain. Following the 12-month booster dose, response rates were 100%, 98%, and 93%, respectively. The study did not examine the long-term persistence of the antibody response or whether the vaccine reduces carriage and thus is able to induce herd immunity.

Interestingly, Novartis Vaccines has also announced plans to enroll an adolescent trial for its new MenB vaccine with multiple study arms (5). It is well known that MenB disease has a second “spike” of incidence peaking at around 18 yrs so the company is seemingly focused on its product being more than an infant/toddler vaccine. Moreover, the presence of multiple study arms in the adolescent trial also might indicate the company is testing its antigens with its various adjuvants e.g. IC-31, MF-59 and CpG in order to investigate any broadening of vaccine coverage in this group.

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Beyond MenB, Novartis Vaccines also reported positive clinical trial results for Menveo, its tetravalent conjugated ACWY-CRM vaccine. The data were presented at a late-breaker platform session on May 5 during the 2008 Pediatric Academic Societies (PAS) Annual Meeting in Honolulu, Hawaii (6). Novartis boldly claim that its vaccine gave a superior immune response to its key competitor Menactra which is based on tetanus toxoid (TT) technology rather than CRM. At the moment it is difficult to predict whether these data will translate into advantages in market share and product pricing but at least this move signals the company's willingness to compete aggressively.

Presently, Menveo's most significant feature is that it covers infants under the age of two. By contrast, Sanofi-Pasteur's Menactra is only approved in the US for use in ages 2 to 10 years although the company is pursuing an infant indication (1-2 yrs) with expected filing in the first half of 2009. Also since its introduction in 2005, data suggests that there may be a small increased risk of GBS (Guillian Barre Syndrome) associated with Menactra vaccination in older groups. A confirmatory safety study is ongoing which should report in late 2008 but in the meantime competitors can highlight these negative data. GSK Biologicals are also working on MenACWY-TT which also targets the infant primary series schedule, with a US filing in 2011.

Both sets of recent data presented by Novartis Vaccines not only give renewed encouragement to the medical aspects of meningitis prevention, they strongly determine the future of the company, both being blockbuster opportunities. Although Novartis faces competition from Wyeth and Sanofi Pasteur Men B programs the first filings of these are not expected until at least 2012. To summarize, the most interesting observation is that both programs were originated at Chiron Vaccines, which now under new Novartis management are both racing to the marketplace.

References:

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