XVIII Lancefield International Symposium, Palermo, Sicily – vaccine update

LONDON, UK----12th September 2011----ExpertREACT. The recently held XVIII Lancefield meeting in Palermo, Sicily confirms the industry is further ahead in Group B Streptococcus than Group A Streptococcus in terms of vaccine development. For GBS, Novartis Vaccines drives an ambitious, global agenda. R&D capacity appears to be limiting others.

Once again the global scientific/medical community with an interest in the *Streptococcus* met in Palermo, Sicily (4 – 8th September) to discuss current issues and progress in the field. It has been 3 years since the last Lancefield held in Porto Heli, Greece. **VacZine Analytics** was in attendance at both meetings and reviews conference highlights, particularly in new vaccine development.

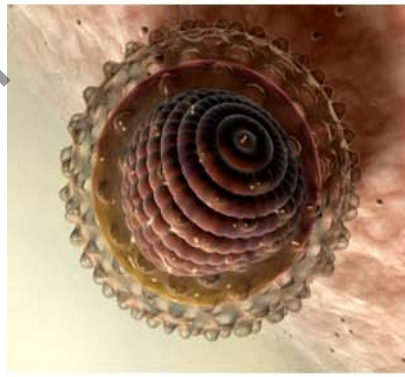
For Group B Streptococcus *(Streptococcus algalactiae),* Prof Carol Baker (US) reminded attendees, that although our understanding regarding global burden of disease was still limited in developing/emerging regions, in the West the pathogen remained high priority for new vaccine development. GBS, responsible for neonatal early onset and late-onset disease (EOD/LOD), caused >85% of bacterial meningitis cases in < 2 months according to US data from 2003-2007; far exceeding other important pathogens *Streptococcus pneumoniae* and *Neisseria meningitidis* **(1)**. The latter become more significant if one examines the data in older children (> 2 mos) but in all pediatric cases (0 – 17 yrs) still GBS comprises a significant proportion (~40-45%) of cases. Previous data from the Active Bacterial Core surveillance (ABC)/Emerging Infections Program Network (1999-2005) suggests that GBS is also an important pathogen in adults/elderly with incidence (5 cases per 100,000 population 15-64 yrs) in 2005 increasing 48% since 1999 **(2).** Considering these data, especially in children, a interesting point raised at the meeting was that GBS incidences are seemingly higher than those of *Haemophilus influenza* type b prior to vaccine introduction.

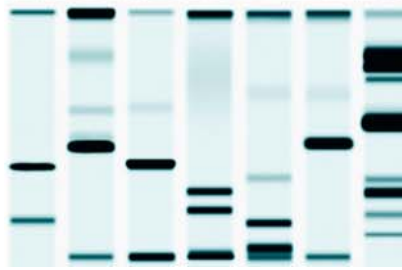
Novartis Vaccines are actively developing a trivalent glycoconjugate GBS vaccine composed of serotypes Ia, Ib and III. At the meeting, the company (K. Slobod, USA) gave a first significant public update regarding status of the program, currently in Phase I testing. Novartis predicts its vaccine will cover 65%, 86% and 85% of EOD serotypes in US, S.Africa and Malawi respectively, with higher respective coverage rates in LOD. In its V98_06 Belgium study, the GBS vaccine (1 dose, 5μg/5μg/5μg) was shown to be immunogenic (Day 61 GMC, 95% CI) with no further benefit of an additional dose or alum. NVS presented a path to licensure strategy which involved the eventual inclusion of a >50,000 Phase III efficacy trial in pregnant women. The final location of the efficiacy trial is being investigated by planned epidemiologic studies in Hong Kong, Dominican Republic, Panama and Bangladesh where enough GBS cases should be observed in each study arm to see a statistically signficiant vaccine effect. A first pilot of the efficacy trial (V98_07) could begin in 2012.

Many within the GBS field accept that the fear of litigation using pregnant women as a target population has hindered GBS vaccine development. Currently, only influenza and in some regions, tetanus vaccines are recommended for administration to pregnant women. The case is also being advocated for pertussis **(3).** Due to large burden of GBS disease in < 2 mos, the NVS strategy of developing a maternal vaccine with “early protection” is therefore medically sound but surprisingly bold and risky. Aside from safety considerations, by conducting a large Phase III efficacy trial NVS will lay down vaccine proof-of-concept so supporting competitors in their production of “me too” GBS vaccines. Other companies, notably Pfizer (Wyeth) have great expertise in CRM197 polysaccharide conjugation.

The Novartis program also is distinctly global from the outset; again logical since many references/posters at the Lancefield meeting suggested the burden of GBS disease in developing countries was similar to the West. The NVS vaccine does not currently include a serotype V component, which accounts for around ~18% of EU GBS isolates as indicated by preliminary data released at the Lancefield by the DEVANI consortium **(4).** Broader vaccine coverage could be addressed by a second generation vaccine which could involve additional of recombinant GBS pilus proteins also presented at the meeting **(5).** One could speculate that the lower potential coverage of the trivalent approach in US (~65%), normally the most lucrative vaccine market, has forced NVS to think about disease burden outside the major seven economies.

CONTINUED……





CONTINUED……

The fact that the potential NVS GBS vaccine would be a single shot meets the ideal profile also for mass vaccination campaign in developing regions.

The development of new vaccines for Group A Streptococcus (GAS) were also covered at the meeting. In terms of a commercial candidate entering clinical testing, the field had advanced less than GBS. Against a backdrop of conference speakers reiterating the huge burden of Group A Streptococcus related diseases e.g. Rheumatic heart disease (RHD) and indeed, the continued unpredictability of the pathogen exemplified by recent Scarlet fever outbreak in Hong Kong **(6)**, the need for a GAS vaccine remains as strong as ever. In an opening talk, Prof Johnathan Carapetis (Australia), advocated a new five year plan to tackle GAS diseases which involved development of a vaccine ideally to prevent childhood pharyngitis. In his view, increasing interest and discussion at global bodies such as the WHO, Hilleman Institute and the Decades of Vaccination effort **(7)** is encouraging – but he questioned the hesitance of industry.

For academic vaccine efforts, a revised 30-valent "Strepavax" vaccine composed of 4 new polypeptides targetted to North American pharyngitis was discussed (J.Dale). 30-v is "predicted to enter Phase I in the near future" and in early rabbit studies was show to evoke bactericidal antibodies against both vaccine and non-vaccine serotypes. Other programs discussed included two from Australia (McMillan DJ, Good M) and one from Brazil ("Streptincor", Guilherme L) all targetting the C-terminal region of the GAS M-protein. Professor Good presented published data indicating the vaccine (J8-DT/alum) could provide protective immunity (with memory responses) against both skin/throat GAS strains in a new superficial skin model mimicing GAS pyoderma **(8)**. Again, J8-DT which now receives support from the NIH, is predicted to enter Phase I soon.

Apart from a discussion on detoxified GAS Streptolysin O **(9)**, neither Novartis Vaccines or Pfizer gave any significant update on GAS vaccine preclinical programs which previously we have stated to be ongoing. This may confirm the meeting sentinment that industry interest is low – but in reality both companies are capacity limited by progress in exactly the same programs: *Neisseria meningitidis* serogroup B and *Staphylococcus aureus*.

References and Notes:

1) Thigen MC et al. Bacterial Meningitis in the United States 1998-2007. N Engl J Med 2011 364; 21
2) Phares CJ et al. Epidemiology of Invasive Group B Streptococcal Disease in the United States, 1999-2005. JAMA. 2008;299(17):2056-2065.
3) Brady T. CDC supports administration of pertussis vaccine during pregnancy. AAP News 2011; 32:19
4) Efstratiou A – on behalf of the DEVANI Study Group. PAN-European screening study for *S.agalactiae*. XVIII Lancefield International Symposium. Palermo, Italy 4 – 8 September 2011
5) Maione D on behalf of the DEVANI Study Grou – Pili genes pattern in Group B Streptococus from newborn infections and pregnant women in Europe (DEVANI project). XVIII Lancefield International Symposium. Palermo, Italy 4 – 8 September 2011
6) Scarlet Fever hits Hong Kong. BBC News Website. Health Section. 21 June 2011. Available at: http://www.bbc.co.uk/news/health-13858115. Accessed August 2011
7) Bill and Melinda Gates Foundation. Bill and Melinda Gates Pledge $10 billion in Call for Decades of vaccines. Available at: http://www.gatesfoundation.org/press-releases/Pages/decade-of-vaccines-wec-announcement-100129.aspx. Accessed August 2011
8) Pandey M et al. Mechanism of protection induced by group A Streptococcus vaccine candidate J8-DT: contribution of B and T-cells towards protection. PLoS One. 2009;4(4):e5147. Epub 2009 Apr 2
9) Chairot E et al. XVIII Lancefield International Symposium. Palermo, Italy 4 – 8 September 2011

A printable version of this article is available upon request.