Immune Correlates of Protection Against Influenza A Viruses in Support of Pandemic Vaccine Development

December 10 and 11, 2007

Panel Discussion

Antigen-specific immune responses in humans

- Is there agreement on immune response priorities to evaluate vaccine immunogenicity and efficacy?

- What about criteria for NA content in vaccines and NA responses?

- What is needed to implement novel measures of binding antibody that are strain specific?

- What qualities of antibody and T cell responses should be measured?

- What additional studies are needed to further define immune parameters that correlate with protection against seasonal influenza? (Comparison of LAIV and TIV)

- Do we need to define correlates of protection for different age groups?

- How can we study the contribution of the innate immune responses and how they relate to protection?

- Why is H5 a poor immunogen?

Preclinical models and surrogates of vaccine efficacy

- How should animal studies be designed to provide meaningful data about vaccine's potential effectiveness against pandemic virus (what should be used as challenge virus, challenge dose, disease signs, immunologic end-points)?

- What information is outstanding that can be gathered from animal studies? Examples are the contribution of innate responses to virus clearance and development effector and memory responses; determination of surrogate markers of protective immunity. Any others?

- Primary human epithelial cells provide one model that should be exploited to understand the level of attenuation of live vaccines and the key virulence factors of newly emerging strains. Any comments?

- More needs to be done looking at vaccine effect on severity of illness. Uniform definitions of: influenza associated illness (what is role of PCR?), lower respiratory tract illness, hospitalization, death. Can we agree on uniform severity score?

Vaccination strategies

- What are the components of an optimal inactivated vaccine? Do we need comparative clinical trials? Will animal models be useful?
- How do we compare contribution of adjuvants and vaccine formulations to vaccine immunogenicity/efficacy?
- Is a multiclade or clade-specific vaccine really necessary?
- Should we develop a vaccine for prepandemic use?
  - Should it be polyvalent? Which HA subtypes should be included?
  - This could prime the immune response, overcoming the need for a 2 dose vaccine regimen after a pandemic has begun.
  - What data should be collected to support approval of a pre-pandemic vaccine?
- What lessons were learnt from past pandemics that can guide development of an effective H5N1 vaccine?
- What opportunities have been missed in development of an effective H5N1 vaccine since 1997?

- What are the characteristics of the ideal clinical trial?
- What outcome criteria should be used for these trials? Immune measurements? Efficacy measurements?
- More needs to be done looking at vaccine effect on severity of illness. Uniform definitions of: influenza associated illness (what is role of PCR?), lower respiratory tract illness, hospitalization, death. Can we agree on uniform severity score?
- Overall sense that a program is emerging to systematically evaluate new vaccine candidates. Can we coordinated evaluation of candidates between Europe and U.S.?