Immunobridging for evaluation of filovirus vaccines

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What is immunobridging?

An inference of effectiveness based on immunological endpoints that compare immunological results with a new vaccine/formulation/subgroup with immunological results in a situation with known efficacy.

Success criteria should account for desired relative efficacy of the new vaccine/formulation/subgroup vs. the comparator.

It is implied that the immunological endpoint (most commonly, binding or neutralizing antibodies) will predict other important components of the immune response. Because a comparison is made, this does not necessarily require a cutoff.

Immunobridging only works if there is a comparator with known efficacy. Access to comparators is essential.

Immunobridging (using a functional Ab or titer) is frequently used to make scientifically appropriate regulatory decisions, but does not necessarily require a CoP as most people define one.
How far is an (immuno)bridge too far?

Same vaccine, similar formulation
Same vaccine, different formulation
Same vaccine, different subgroup
Same vaccine, different antigen (how different?)
Similar vaccines (e.g., similar platforms)
Different vaccines or different pathogen (e.g., strain)

Situations in green are usually well-accepted, others may sometimes be accepted
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- There is increasing acceptance of immunobridging for COVID vaccines, including for variants

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Immunological considerations for immunobridging

What are the protective immune responses likely to be?

Will the chosen immune marker adequately predict the protective immune response for mild & severe disease?

Fc dependent and memory B cell dependent humoral responses, and CMI, are more likely to have their major impact on severe disease.
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Memory responses lead to rapid increase in immunity after exposure.
When would immunobridging more likely predict effectiveness of new vaccines for new viruses?

Responses to vaccines are similar quantitatively and qualitatively
Mechanisms of protection are similar
Timing/kinetics of infection/pathogenesis of the virus is similar
Immune evasion abilities of the viruses are similar (or greater for the comparator)
Immunobridging from ZEBOV to SUDV?

These are different viral species, so there may be a presumption of substantial difference. Nonetheless, there are important similarities:

- **Virology**: similar genomic organization
  - same cellular receptor (with similar conformation of binding)
  - both produce sGP, which may play a role in immune evasion
- **Similar kinetics of infection**
- **Similar chemokine & immune responses**
How could animal data support clinical immunobridging?

Animal studies can:

• Provide support for similarity of disease pathogenesis across different viruses
• Provide support for similarity of protective immune responses across different antigens/viruses
• Provide basic information about protective efficacy of vaccines against different viruses
• Allow dissection of immune system components, e.g., via transgenic animals and passive transfer studies

While animal data could provide strong support for immunobridging, this likely would not be “animal rule” since the primary data would come from comparisons of human immune responses

N.B. There are differences between animal vs. human pathogenesis of disease
Regulatory pathways for demonstrating efficacy

In the US, “traditional approval” can be based on clinical studies or a well-established immune marker that predicts protection.

“Animal rule” and “accelerated approval” are based on “reasonable likelihood of clinical benefit” standard in each case:
- Additional specific criteria apply
- Additional post-marketing data would be needed

Other countries have similar mechanisms.
Conclusions

For platforms with known efficacy against a filovirus, data to support immunobridging to support efficacy of new antigens (within the same platform) against different filoviruses could be obtained.

If comparable immune responses could be demonstrated, and if there were data supporting the likelihood that comparable immune responses would lead to comparable efficacy, this might show reasonable likelihood that a new vaccine would be effective.

There has been skepticism about immunobridging to new platforms for filoviruses.