Infectious Diseases

HRV vaccines and treatments

Human rhinoviruses (HRV) are the most commonly isolated viral pathogens in people suffering with 'the common cold'. Over 150 antigenically distinct types of HRV are currently known and these serotypes span three species: HRV A, HRV B, and HRV C. Rhinovirus infection primarily results in mild, upper respiratory tract disease (approximately 50% of all URTIs) and infection rates among young children can be as high as 8–12 times a year. HRV infections are known to be an important predisposing factor to conditions such as sinusitis, otitis media, bronchitis and primary pneumonia; frequently progressing to secondary bacterial infections in the elderly (5-30%). Rhinovirus infections in care homes have been associated with increased requirements for oxygen therapy and result in longer periods of hospitalisation and higher rates of mortality over influenza. In addition, rhinovirus infections may trigger asthma attacks in children and this predisposition may persist into adulthood.

VALIDATED HRV MODELS

Over 1,500 subjects have been safely infected with HRV to date as part of a controlled human infection study and the HRV model is widely accepted and practiced across the world in the investigation of new treatments for the common cold, asthma and COPD. A GMP manufactured HRV16 strain is the most commonly used and validated rhinovirus for use in human challenge trials.

Challenge with HRV16 produces infection in up to 90% of susceptible volunteers. Symptoms usually first appear within 24 hours after inoculation and peak at 48-72 hours. The clinical syndrome is comparable to that reported in natural colds. Approximately one-third of rhinovirus infections, whether natural or experimental, are asymptomatic. HRV16 challenge may be used to test both prophylactics (i.e. drugs and vaccines that prevent infection and disease) or therapeutics (i.e. mainly drugs used to treat disease once an infection is established).

HRV Vaccines

Conceptual Challenges

Demonstrating efficacy of novel vaccines in the field is time-consuming, costly and associated with risk

- Initial exposure to virus unknown
- Variation in circulating strains
- Large study size and duration
- Difficult to power for clinical efficacy
- Seasonality limitations
- Biomarker identification difficult

hVIVO Human Challenge Models:

Towards a deeper understanding

- Effective exploration of vaccine efficacy and correlates of protection
- Match study design to product mode of efficacy plus high attack rate
- Immunological assays
- Host Response analyses

Primary & Secondary Endpoints:

- Viral area under curve (vAUC)
- Reduction in incidence of symptomatic infection
- Reduction in disease severity

Antiviral/Treatments

Conceptual Challenges

Establishing efficacy of antivirals in early clinical trials is challenging where disease states and relative risk alter with age

- Timing of initiating exposure to virus unknown
- Dose ranging and timing difficult
- Comorbidities and other confounders
- Frequent coinfection
- Seasonality limitations

hVIVO Human Challenge Models:

Towards a deeper understanding

- Study design matched to investigational product mechanism of actions
- Optimisation of treatment timing
- Time-dependent measurements of biomarkers
- Triggered-dosing options (time or virological)
- Controlled strain exposure
- Consistent placebo response
- Efficient resistance monitoring

Immunomodulator

Conceptual Challenges

Demonstrating clinical efficacy in early stage field trials is challenging where initial exposure to virus is unknown

- Baseline prior to infection unachievable, difficult to establish host response
- Effect with/without standard of care treatment difficult to establish
- Large study size and duration
- Circulating strain variation
- Biomarker identification difficult

hVIVO Human Challenge Models:

Towards a deeper understanding

- Well controlled environments
- Baseline well established prior to infection
- Appropriate for both prophylaxis and treatment
- Flexible dosing and timing
- Establish safety and efficacy to impact infected subjects host response
- Investigate and demonstrate target engagement
- Controlled combination-treatment with drug and standard of care or antivirals