Advancing Drug Development for the Prevention and Treatment of Respiratory Syncytial Virus Infections
Marriott Marquis • Washington, DC
May 2, 2016

Meeting objectives: The objectives for this event are to: 1) explore possible definitions for respiratory syncytial virus (RSV) disease severity; 2) identify and discuss populations that will be evaluated in clinical trials; 3) identify and discuss clinically meaningful endpoints to be used to assess efficacy of drugs designed for prevention and to treat illness due to RSV; 4) describe nonclinical and clinical approaches to developing products that will be primarily used in the pediatric population; 5) explore the types of proof-of-concept data needed to initiate clinical trials in infants and young children; and 6) discuss RSV drug development for other populations, such as elderly and immunocompromised patients.

9:00 a.m. Welcome, Overview, and Meeting Objectives
Greg Daniel, Duke-Margolis Center for Health Policy

9:15 a.m. Opening Remarks
Jeff Murray, US Food and Drug Administration

9:30 a.m. Facilitating Drug Development for Treatment of Respiratory Syncytial Virus (RSV) Infections
Alan Shapiro, US Food and Drug Administration

9:45 a.m. Session I: Issues Related to RSV Bronchiolitis Treatment Trials Establishing Definitions and Identifying Endpoints

Session 1a: Establishing Definitions of At-Risk Populations and Disease Severity
Moderator: Greg Daniel, Duke-Margolis Center for Health Policy

Opening Presentation: Robert Welliver, University of Oklahoma Health Sciences Center

- How do we define disease severity in the population to be studied (e.g., “moderate” disease, “severe” disease, or all symptomatic illness)?
- What other factors are important in defining the study population (e.g., chronological age, underlying risk factors for severe illness, upper versus lower respiratory tract illness)?

Discussion (30 minutes)

10:30 a.m. Break

10:45 a.m. Session Ib: Identifying Appropriate Endpoints for RSV Bronchiolitis Treatment Trials
Moderator: Greg Daniel, Duke-Margolis Center for Health Policy

Opening Presentation: Cody Meissner, Tufts University School of Medicine (10 min)
Panelists:
- Selena Daniels, U.S. Food and Drug Administration (5-7 min)
- Jason Chien, Gilead Sciences (5-7 min)
- Barbara Rath, International Society for Influenza and Other Infectious Diseases (5-7 min)
- Flor Munoz, American Academy of Pediatrics (5-7 min)

Questions to address:
- Which signs and symptoms should be included in an instrument used to capture clinical severity of RSV?
- What should the primary outcome measurement be to establish treatment efficacy? Time to reach a pre-determined score? Change in score on a pre-determined day of illness? Other possibilities?
- Can the same signs and symptoms (or the same instrument) be used for study inclusion criteria and for establishing treatment response?
- Are two symptom instruments needed to measure treatment response: one for clinicians and one for caregivers? How would they be combined in an endpoint?
- Is there support among the pediatric and infectious disease community for validating a clinical tool to measure disease severity for RSV illness among infants (e.g., < 12 months of age)?
- Are there potential secondary endpoints that might be considered clinically meaningful and supportive (e.g., RSV viral load, biomarkers)?

Discussion (65-75 minutes)

12:30 p.m. Lunch

1:30 p.m. Session II: Identifying Alternative Endpoints for Prevention of RSV Bronchiolitis
Moderator: Mark McClellan, Duke-Margolis Center for Health Policy

Opening Presentation: Jeff Roberts, US Food and Drug Administration (15 min)

Questions to be addressed:
- Should a novel prophylaxis product prevent all symptomatic RSV-related illness or only the most severe manifestations? What degree of illness-reduction is clinically meaningful?
- Given the differences in natural history of the illness in different populations, are different endpoints needed for different populations (i.e. healthy infants, premature infants, or those with underlying conditions)?
- The pivotal studies supporting approval of palivizumab employed hospitalization as the primary endpoint, which may no longer be the ideal endpoint, making a non-inferiority margin based on previous palivizumab trials difficult to justify. What is the best way to assess novel prophylaxis products in the context of the approved product?
• To what extent can prophylaxis efficacy from one group of infants be extrapolated to another? For example, can efficacy in healthy full-term infants be extrapolated to infants at higher risk of severe illness (e.g. prematurity, chronic lung disease, congenital heart disease)?

**Discussion (30-45 minutes)**

2:30 p.m. **Session III: Initiation of Pediatric Trials for RSV Bronchiolitis**  
*Moderator:* Mark McClellan, Duke-Margolis Center for Health Policy

*Opening Presentation:* Prabha Viswanathan, US Food and Drug Administration

*Questions to be addressed:*
  • What types of proof-of-concept studies are needed to support initiation of pediatric studies for treatment and prevention products?
    • Which adult populations/disease conditions are preferred?
    • To what extent can non-clinical data be used to support pediatric studies (i.e., animal models of disease)?
    • Are adult challenge studies adequate to demonstrate proof-of-concept for infant bronchiolitis trials?

**Discussion (30 minutes)**

3:15 p.m. Break

3:30 p.m. **Session IV: Encouraging RSV Drug Development in Other Populations**  
*Moderator:* Mark McClellan, Duke-Margolis Center for Health Policy

*Panelists:*
  • Filip Dubovsky, MedImmune/AstraZeneca *(5-7 min)*
  • Edward Walsh, University of Rochester *(5-7 min)*
  • Michael Boeckh, Fred Hutchinson Cancer Research Center *(5-7 min)*

*Questions to be addressed:*
  • How do we encourage RSV drug development in other populations such as elderly or immunocompromised patients?
    • What are the unique considerations for trials in older children and adults? Are different endpoints required?
    • What is the optimal approach to studying small populations such as stem cell transplant populations, in which the sample size may be small and controlled trials are difficult to conduct?
    • Should both prophylaxis and treatment be evaluated in non-pediatric populations?

**Discussion (25-30 minutes)**
4:15 p.m.  **Identifying Next Steps**  
Mark McClellan, Duke-Margolis Center for Health Policy

4:30 p.m.  **Closing Remarks**  
Mark McClellan, Duke-Margolis Center for Health Policy

4:45 p.m.  **Adjournment**

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