ABDD-QbD HABP/VABP Trial Design Meeting: Summary of Top Challenges

Brad Spellberg, MD  FIDSA  FACP
Associate Professor of Medicine
Geffen School of Medicine at UCLA
Associate Medical Director for Inpatient Services
Division of General Internal Medicine
Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center

Disclosures
Grant & Contract Support: NIH, Cubist, Pfizer, Eisai, Bristol Myers Squibb;
Consultant: Glaxo Smith Kline, Meiji, Cardeas, Affinium, aRigen, Synthetic Biologics
Recommended Design Features of Future Clinical Trials of Antibacterial Agents for Hospital-Acquired Bacterial Pneumonia and Ventilator-Associated Bacterial Pneumonia

IDSA; ACCP; ATS; SCCM

- Result of a 2 day FDA-IDSA-ACCP-ATS-SCCM workshop held in Silver Spring, MD on March 31-April 1 2009
- This was a follow on to a 2 day CAP workshop the previous year
- Industry participation at both meetings
Ongoing Discussions

• Sponsors have continued to try to plan for such studies

• At least one study has been successfully completed in this space, focusing on MRSA (Wunderink et al, ‘12 Clin Infect Dis 54:621-9)

• November 29, 2012 FDA Anti-Infective Ad Board
Contentious Areas

• Pre-study antibiotics
• Primary efficacy endpoint and NI margin
• How sick must enrolled patients be?
• Can HAP and VAP be studied at the same time?
• What comparator drugs should be used?
• What is the evaluable population?
• How is micro confirmation done?
Group Identified Discussion Points

Patient Enrollment

- Disease severity criteria for inclusion
- Standardizing the definition for HABP/VABP
- Pre-study AB drug use
- Pre-study micro evaluation
- Informed Consent issues
Efficacy and safety outcomes

- Considerations for a hierarchical endpoint with clinical criteria
- Pre-study AB drug use time period (wrt mortality EP)
- NI margin, sample size and mortality rate
- Criteria for comparator drug
- Target severity/ comorbidity criteria for mortality rate, and stratification to balance arms
- Safety outcomes (and safety reporting)
Evaluable population and analysis

- Method of microbiology confirmation
- Microbiological criteria for inclusion in evaluable population (% micro confirmed for micro-ITT and analysis)
- Allowed concomitant AB drugs