



Antibacterial Drug Development an FDA Perspective

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Background

- Development of new antibacterial agents is essential to meet patient needs
 - Need therapies to treat patients with infections today
 - Know we will need new options in the future
- Two development prongs - ideally
 - Unmet need – trying to catch up to meet critical public health needs in areas where we are behind
 - Ongoing development – so new options are available to address the needs that we know will arise in the years ahead

Challenges in Studying Antibacterial Drugs

- Biology of the acute bacterial infectious diseases
 - Acute illness - Early doses important
 - Urgent need to initiate therapy for serious infections
 - Diagnostic uncertainty
 - Micro diagnosis – time delayed – detection limits of common techniques – better diagnostics could help
 - Effects of prior therapy or concomitant therapy – may cloud assessment of the test drug (NI trials)
 - Heterogeneity in outcomes dependent upon multiple factors (e.g., patient factors)
- Limitations of the available information on natural history of disease to estimate treatment effect
- Different compared to many other therapeutic areas

Antibacterial Drug Development

- Extent and breadth of antibacterial drug development seems below level needed to meet patient needs
- Limited development activity in some therapeutic indications
- Balancing precision of assessments of safety and efficacy with feasibility & public health need for new options – areas of unmet need
- Tools & approaches to facilitate study of new antibacterial drugs

Unmet Need

- Serious or life-threatening bacterial infections where patients lack satisfactory therapeutic options
- Risk / Benefit in the setting of unmet need
- More streamlined development – get drugs to patients sooner in areas of unmet need
- Greater uncertainty / risk with a more limited development program
- An indication that reflects the more limited development program – targeting use in settings where other available drugs not satisfactory

Unmet Need – Data Sources

- Preclinical Data – what role can this data contribute?
 - Mechanism of action / impact of resistance to other drugs
 - Animal models of infection
- Clinical Data
 - PK data to estimate appropriate dosing in indicated population(s)
 - Data from a trial in patients with serious or life-threatening infections (role of patients with “susceptible” infections)
 - Approaches to analyzing data from across multiple body sites
 - Clinical trial may enroll patients with organisms resistant to other therapies and patients with organisms susceptible to other therapies
 - Degree of precision of estimates of safety and efficacy if indication is for patients who lack satisfactory treatment options
 - Additional data from limited experience in patients with limited therapeutic options b/c of “resistant” organisms

Tools

- Better means to evaluate safety and efficacy
- Can we learn more from the data that is accrued during development?
- Can Bayesian approaches help?
- Approaches to analyzing data in a trial enrolling patients with infections from across multiple body sites
- Can endpoints be further developed and standardized to facilitate and enrich development?
- Are there clinical trials procedures that are being done that do not add value?
- Can clinical trial networks facilitate the study of antibacterial drugs given the inherent challenges in studying antibacterial drugs for these acute diseases



Thank you