Public Workshop
Developing Antibacterial Drugs That Target a Single Species

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Welcome

Public Workshop — Developing Antibacterial Drugs That Target a Single Species

- An opportunity for discussion
- Not an Advisory Committee
- Conflict of interest disclosures available
- Open time for public comment

Panel Introductions

Agenda

Time	Topic	Presenter
8:30-8:45	Introduction	Ed Cox
8:45-9:00	Overview of Case Study	Peter Kim
9:00-10:30	Perspectives on the case	
	Academia	Helen Boucher
	Industry	John Tomayko
	FDA	Sumathi Nambiar
	EMA	Marco Cavaleri
10:30-10:45	Break	
10:45-11:15	Clarifying Questions (Panelists and Audience)	
11:15-12:15	Presentation of the Clinical program	John Rex
12:15-1:00	Lunch	
1:00-1:30	Clarifying Questions (Panelists and Audience)	
1:30-2:00	Public Comments	
2:00-3:45	Panel Discussion	
3:45-4:00	Next steps/concluding remarks	Ed Cox

Developing Drugs Targeting a Single Species

- Can do if species occurs with at least a moderate degree of frequency
  - skin infections caused by *S. aureus*
- Challenging if species of interest occurs infrequently
  - Number of patients needed using usual statistical conventions for an infrequently occurring species exceeds what likely can be achieved in relevant time frames
- Rapid diagnostics very important
  - can help guide clinical use of such a species specific therapy and support prudent use
  - can help, but won't solve the challenges of clinical trials for infrequently occurring species

Drugs Targeting a Single Species

- Some investigational agents target a single species that causes disease infrequently
- Drugs active against only a single species should have less of an effect on normal flora
  - will they promote resistance less than broader agents?
  - less alteration of normal flora and less shifting of flora to more resistant bacteria and fungal colonization that may lead to infection?
  - will we see less *C. diff* colitis?
- What would the clinical role be for such a drug?

Disease Characteristics and Trial Designs

- Serious acute bacterial diseases
- Oncologic conditions
- HIV/HCV
- Rare metabolic disorders

  - Identifying patients
  - Disease course over time
  - Diagnostic certainty
  - Urgency to initiate therapy
  - Variability in outcomes and time to clinical outcome
  - Opportunities for rescue therapy for patient not responding

What to Do When Species of Interest is Infrequent?

- Less precise estimates of efficacy / greater uncertainty
- May not achieve usual statistical conventions
- Particularly challenging where outcomes for serious acute bacterial disease are variable depending on factors known and unknown
- Effects are not “lights on vs. lights off” e.g., a shift from 90% to 10%

Evaluating Efficacy

- Options for discussion include:
  - accepting greater uncertainty from clinical data?
    - small numbers of patients
    - concomitant therapy
  - if clinical trials not feasible / practical
    - animal rule to evaluate efficacy?
    - safety data from humans
    - provisions for restrictions on conditions of availability
  - other ideas?

Animal Models for Evaluating Efficacy Under the Animal Rule

- Predictive of response in humans – not just to measure activity
- Is there a "good animal model of infection"
- Lots of difficult questions
  - which species?
    - similar or different susceptibility
  - what inoculum?
  - when to intervene with test drug?
  - animal may metabolize/clear drug differently

Discussion

- Pros and Cons of different potential pathways for development
  - Clinical data
  - Animal data
- Important to have a pathway for development so that the potential for such drugs for treating patients can be evaluated

- Thank you