BARDA'S MARKET RESEARCH FOR A CLINICAL TRIAL NETWORK FOR ANTIBIOTICS

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Disclaimers

- I am an employee of the US Federal Government
- I have no conflicts of interest

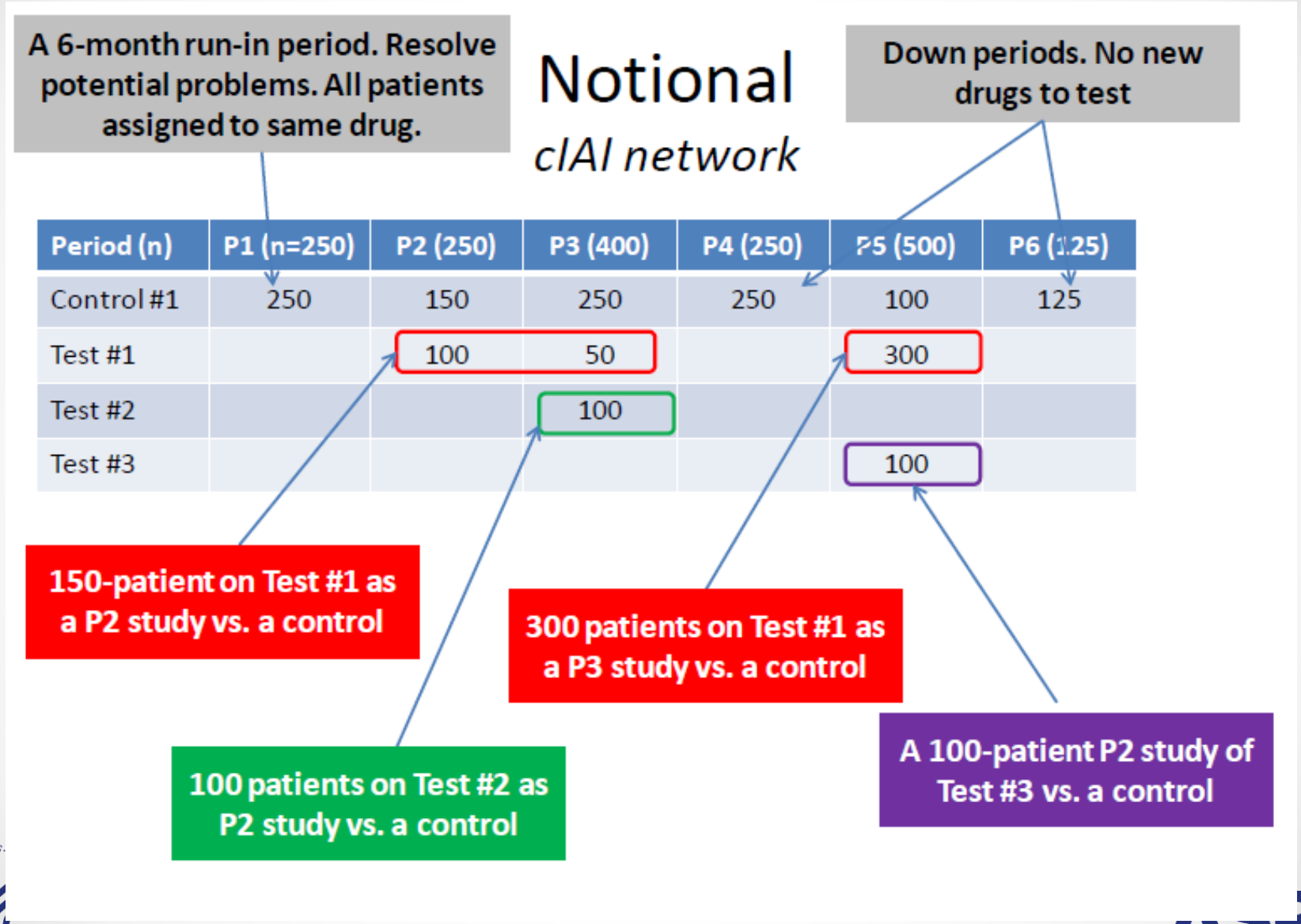
BARDA

- BARDA supports PPPs for the development of new antibacterial drugs
- We have been involved in one way or another in Phase III clinical trials for Achaogen, Tetraphase, Rempex, and Cempra.
- We anticipate being involved in the Phase III clinical development of BARDA supported programs with AstraZeneca, GSK, Basilea and others.

Another Problem/Opportunity (as BARDA sees it)

- BARDA supports each of its clinical trials independently
- Thus, we build (and pay for) the infrastructure to conduct these trial each time we want to conduct one
- Could efficiencies be realized thru consolidation/coordination of these efforts?

Clinical Trial Network



Overview

- As a first step, BARDA conducted market research
  - Obtain technical approach and cost/pricing data
- RFI issued on February 4th
- Responses received April 11th
- 11 Responses
  - 8 CROs with technical approach and cost data
  - 3 responses from companies developing antibiotics with comments/concerns/risks

Cost Data Assumptions

- 10 year period of performance
- Following an initial set up period (~1 year)- 3 antibiotic candidates in the ADCTN per indication annually.
- Cost data broken out for each indication, i.e. cost data for the network to study 3 antibiotic candidates for cUTI only, cost data for the network to study 3 antibiotic candidates for cIAI only, cost data for the network to study 3 antibiotic candidates for HAP/VAP only.
- Rough order of magnitude cost estimates are acceptable. The Responder shall provide their projections based upon a target capacity for Phase 2 and Phase 3 studies of 500 and 1,000 enrolled patients per year for cIAI, 500 and 1,000 enrolled patients per year for cUTI and 300 and 600 enrolled patients per year for HAP/VAP.

Caveats to Cost Data

- Indirect costs not reported in many responses
  - Estimates suggest this would increase cost by approximately 35%
- Different responses used different assumptions
- Investigator costs not included in certain responses
  - BARDA clinical staff estimate this would increase estimates by 40-60%

Summary of Annual Costs

Study	cUTI 500 patients	cUTI 1000 patients	cIAI 500 patients	cIAI 1000 patients	HABP/VABP 300 patients	HABP/VABP 600 patients
Mean cost	$19.4M	$33M	$21.2M	$33.3M	$19.8M	$31.2M
Max	$26M	$52M	$26M	$52M	$42M	$59.5M
Min	$13M	$21.2M	$13M	$24.5M	$7.8M	$31.2M

Warm Base Costs

- Mean: $37.9M-$55.7/annually
- Max: $50-82M
- Min: $22.3M-$36M

Responder	cUTI 500/1000 Patients	cIAI 500/1000 Patients	HABP/VABP 300/600 Patients	Other
Response 1	90/180	140/275	125/250	
Response 2	100	100	300	
Response 3				75 sites total
Response 4	100	100	100	
Response 5	75/150	150/250	100/175	
Response 6				Not reported
Response 7	200/300	200/250	100/200	
Response 8	153/306	115/229	92/183	
Mean	113/173	125/182	127/183	
Max	200/300	200/275	300/300	
Min	90/100	100/100	92/100	

Governance

- How critical is past experience? In what areas? Setting up CTNs', developing MCPs, specific disease indications, working with RAs?
- Should CTN be network of CROs?
- Who leads the CTN? Some responders recommended that the network be ran by a third party academic group
- What is the organizational structure?

Overarching challenges

- Financing
  - Infrastructure could be built and maintained, but likely would need to adopt of fee for service model
- Are there sufficient products in development to warrant the investment in infrastructure?
- Uncertainty-i.e.-If we build it, will industry participate?
  - Will likely need to fund the entire trial costs of the first few candidates to demonstrate competency and success of the network, then move to fee for service

Common Challenges Identified

- Flexibility in the master protocol
- Regulatory updates, auditing, and compliance
- Selection of standard of care
  - Global standard of care map suggested to aid management
  - Getting sites to agree globally will be a significant challenge
- Endpoint selection
- Data monitoring committees (network vs sponsor)
- Addressing product specific safety and efficacy objectives
- Data blinding
- Dose adjustments
- Handling of Proprietary data
- Database construction and standards
  - Companies already have company specific internal process for case report forms-would require “buy in” on data management processes

Summary

- The annual cost to operate the ADCTN for cUTI, cIAI, and HAP/VAP is estimated to be $60-100M annually.
  - Does not cover start up costs or in some cases indirect costs
  - Does not cover investigator costs
- CTN should be financed at $200M-250M to cover unforeseen risks
  - This included costs to cover all costs and the trial costs for 2-3 antibiotic candidates.
  - Warm base costs are less, but still around $100M
- There are several key challenges regarding the development and implementation of the Antibacterial Drug CTN

Alternative Approaches

- BARDA solicited information on establishing a stand alone network to do Phase II/III clinical trials for traditional antibiotic indications
  - This will be challenging to finance
- Are there other models that could be examined?
- Could a set of existing clinical trial networks in the US and EU be coordinated to accomplish the same goal?
  - Coordination then becomes the challenge

Next Steps

- Identify elements that would be critical to place in any Request for Proposals (RFP)
- Resolve or develop plan to mitigate challenges that have been identified thru RFI process
- Determine the most appropriate governance structure to successfully manage the CTN
- Elucidate path to feasibility/financing-currently a working group ran out of Wellcome Trust

Thank you

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