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BRINCIDOFOVIR
SMALLPOX MEDICAL COUNTERMEASURE

JUNE 8, 2016

RESEARCH TRIANGLE PARK, NC

Smallpox as a Potential Bioweapon

- Considered a Class A threat by PHEMCE
- Two known research stockpiles: US CDC and Novosibirsk, Russia
- Additional stockpiles of virus are likely to exist
  - no international registry of potential stockpiles, no efforts to confirm the destruction of viral stockpiles

- Highly infectious with >30% mortality
- Weaponized virus may include efforts to increase transmission or reduce efficacy of antivirals
- Recent terrorist attacks have demonstrated the potential for the inclusion of radioactive substances
- Routine vaccination discontinued in early 1970s

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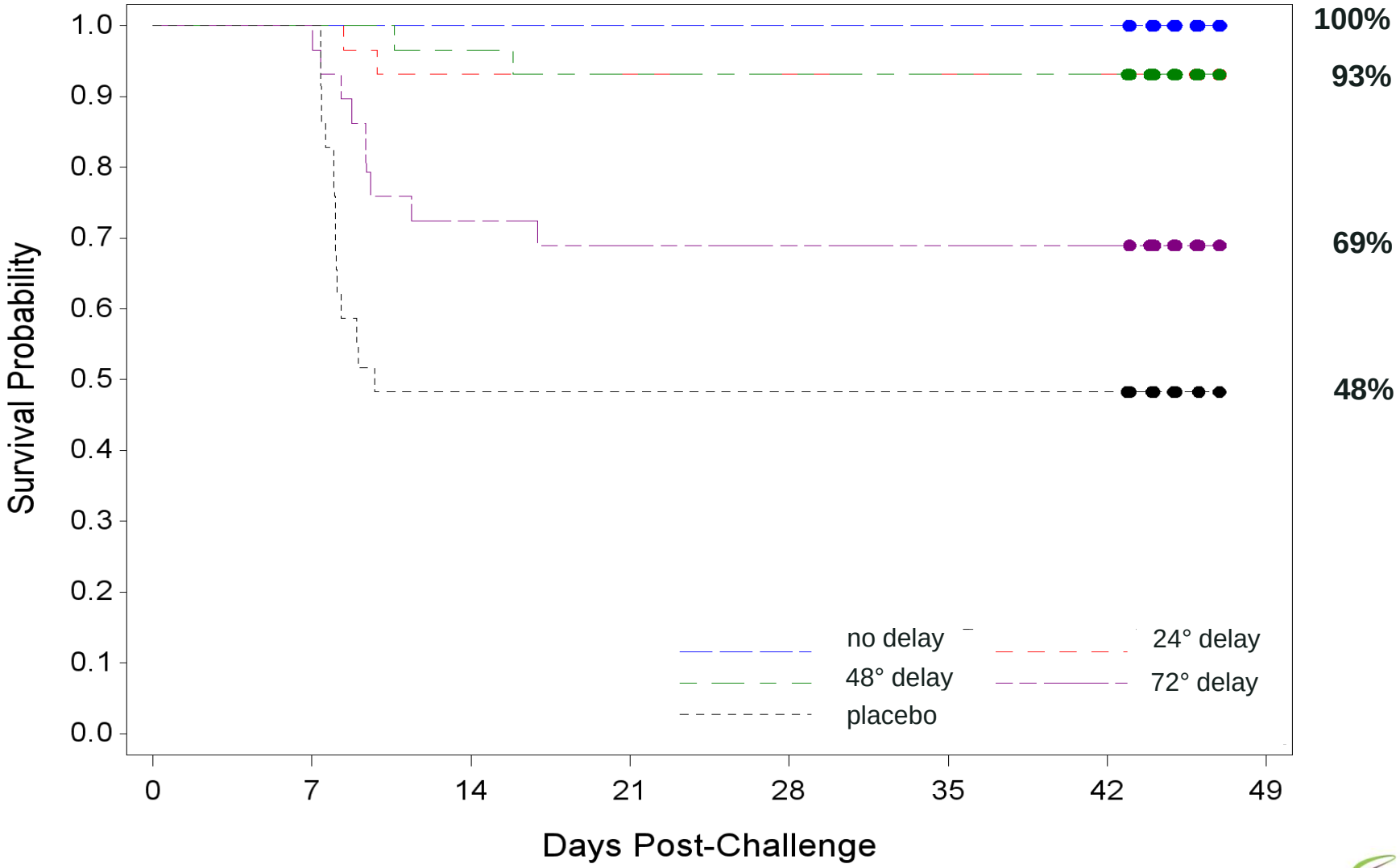
Smallpox Preparedness

- Vaccination is the first line of defense in the event of a smallpox outbreak, but must be administered prior to the onset of disease
- Individuals with certain skin conditions or with immune deficiencies are contraindicated for live virus vaccine
- Institute of Medicine (IOM) recommendation for two antivirals with different mechanisms of action for the CDC's Strategic National Stockpile (SNS)
- Antivirals have demonstrated the ability to treat orthopox infections even after the appearance of clinical signs and symptoms, providing a therapeutic window
- Antivirals may provide therapeutic as well as public health benefit in reduction of infectivity

Brinci: Progress Toward FDA Approval

- Development of brincidofovir as a medical countermeasure for the treatment of smallpox is progressing under the FDA's Animal Rule
  - Allows for the demonstration of efficacy in well-established animal models of disease
- Rabbitpox causes a lethal infection in rabbits, preceded by clinical signs and symptoms
  - Pivotal study complete, demonstrated 100% survival in animals administered BCV at the time of detection of fever
  - Delayed administration provided improved survival over placebo, confirming window of opportunity for therapeutic benefit beyond the midpoint of disease progression

Brinci: Demonstration of Survival Benefit



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Brinci Profile

- Potential Smallpox Utility:
  1. Short course of dosing for post-exposure prophylaxis
  2. Longer course of therapy for treatment
  3. Reduce adverse effects associated with vaccination
- Ease-of-use, low pill burden
  - 100 mg tablets, 1-2 x weekly for adults
  - suspension for pediatric patients
  - intravenous formulation in development
- Large safety database of >1500
  - adults and pediatric patients as young as 2 months
  - immunocompromised individuals

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Smallpox Update: U.S. BARDA procurement

- BARDA posted an intent to procure up to 1.7 million courses of brinci for the Strategic National Stockpile in April 2015
- Although the contract was not able to be finalized in 2015, Chimerix is optimistic that we will be able to re-open negotiations within FY2016
- Broad spectrum of activity against all five families of dsDNA viruses provides additional opportunities for use

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