

CAMO (COMPARING ANIMAL MODELS TO ORGANOID) - TESTING MEDICAL COUNTERMEASURES WITH MICROPHYSIOLOGICAL SYSTEMS AND COMPARING TO TRADITIONAL ANIMAL MODELS AND CLINICAL TRAILS

Marburg Virus Disease In Cynomolgus Monkeys For Development Of Therapeutics

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The potential for Marburg virus (MARV) outbreaks has highlighted the urgent need for approved medical countermeasures for treatment and prevention of MARV disease (MVD). Due to the limited and sporadic nature of MARV outbreaks, the scientific community must rely on well controlled animal studies to assess the potential clinical benefits of candidate therapeutics and vaccines. Here, we describe a natural history study, conducted in compliance with Good Laboratory Practices (GLPs), to characterize the time course and order of progression of the disease manifestations of MVD in cynomolgus monkeys. Furthermore, this well characterized animal model will provide benchmark parameters for comparing and contrasting Microphysiological Systems (MPS) as we effort to find alternatives to animal models. In this study, 12 cynomolgus monkeys were exposed, by the intramuscular (IM) route, to a target dose of 1000 pfu MARV(Angola), and 6 control animals were mock-exposed. Disease manifestations were assessed via blood samples collected from central venous catheters, body temperature and activity measured via telemetry, clinical observations, necropsy, and histopathology. All mock-exposed animals remained healthy throughout the study. Among MARV-exposed animals, systemic inflammation, coagulopathy, and direct cytopathic effects of MARV all contributed to multi-organ dysfunction, failure, and death, with all 12 MARV-exposed animals (100%) succumbing 8 to 10 days post inoculation(PI). Manifestations of MVD that could be used to guide the timing for initiation of treatment in future studies include fever, viral RNA (reverse-transcription polymerase chain reaction [RT-PCR]), lymphocytolysis, coagulopathy, and elevated aspartate transaminase and alkaline phosphatase. In summary, this GLP study provides a detailed characterization of MVD in cynomolgus monkeys that can be used as a foundation for testing MARV countermeasures under the Animal Rule. Additinally, this comprehensive animal study has provided benchmark physiological, chemical and clinical parameters that can be applied to current and development MPS to facilitate assessment of these alternative models in accurately recapitulating animal disease time course and disease manifestations.

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