P0458
Poster Session I
Emerging viruses / viral infections

A PHASE 1, MULTIPLE ASCENDING DOSE STUDY OF AVI-7288, A PMOPLUS® COMPOUND WITH ACTIVITY AGAINST MARBURG VIRUS

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Objectives: The objectives of this clinical study are to determine the safety, tolerability and pharmacokinetics of intravenous (IV) administration of multiple doses of AVI-7288, a phosphorodiamidate morpholino oligomer with positive charges (PMOplus®) that targets the mRNA of Marburg virus nucleocapsid protein. This randomized, double-blind placebo-controlled study was conducted in healthy human subjects over a dose range predicted by studies in non-human primates to cover a therapeutic dose. Marburg hemorrhagic fever (MHF) is a rare human disease caused by Marburg virus, a filamentous, single-stranded, negative-sense RNA virus of the family Filoviridae which is among the greatest bioterrorism threats. No vaccine or established effective therapy is currently available for this catastrophic disease. AVI-7288 has demonstrated evidence of protection against lethal infection in non-human primate models of MHF.
Methods: Up to 40 healthy male and female subjects between 18 and 50 years of age are being enrolled in 5 dose escalation cohorts of 8 subjects each and are receiving 14 daily IV infusions of AVI-7288 at doses of 1, 4, 8, 12 and 16 mg/kg/day, or matched placebo in a 3:1 ratio. Safety is being monitored through adverse event collection, clinical laboratory tests and ECGs. The study is being overseen by an independent Data Safety Monitoring Board (DSMB).
Results: The first 4 dose cohorts have been enrolled and dosed. No significant safety concerns have arisen upon review of blinded study data by the independent DSMB. No serious adverse events have been reported. A variety of adverse events such as headache (n=6 subjects) have been reported; all were mild or moderate in severity.
Conclusions: Preliminary results of this phase 1 study suggest that multiple IV infusions of AVI-7288 are safe and well-tolerated up to a dose level of 12 mg/kg/day. Enrollment of subjects in the remaining dose cohort is ongoing. Unblinded safety and pharmacokinetic data will be presented for all 5 cohorts. ClinicalTrials.gov Identifier: NCT01566877. This work is being conducted under contract with the Joint Product Management Office of BioDefense Therapeutics (BD-Tx), a component of the Medical Countermeasure Systems Joint Project Management Office (JPM-MCS) within the U.S. Department of Defense's Joint Program Executive Office for Chemical and Biological Defense.