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MEETING ABSTRACTS

HUMAN PLASMA-DERIVED BUTYRYLCHOLINESTERASE IS BEHAVIORALLY SAFE AND EFFECTIVE IN CYNOMOLGUS MACAQUES (*Macaca Fascicularis*) CHALLENGED WITH SOMAN

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Organophosphorus compounds (OP) pose a significant threat. Administration of human butyrylcholinesterase (Hu BChE) may reduce or prevent OP toxicity. Thus, we evaluated the safety and efficacy of Hu BChE in monkeys using sensitive neurobehavioral tests while concurrently characterizing absorption and elimination in the presence and absence of high-dose soman exposure to predict time course and degree of protection. Eight young adult male cynomolgus macaques were trained on two distinct automated tests of neurobehavioral functioning. Hu BChE purified under current-Good-Manufacturing Practices (CGMP) was injected intramuscularly at 13.1 mg/kg, producing an average peak plasma value (C_{max}) of 28 Units/ml. The apparent time to maximum concentration (T_{max}) approximated 12 hours and the elimination half-life approximated 80 hours, returning to pre-administration (baseline) levels by 14 days. No behavioral disruptions following Hu BChE administration were observed on either neurobehavioral test, even in monkeys injected 24 hours later with an otherwise lethal dose of soman. Thus, Hu BChE provided complete neurobehavioral protection from soman challenge. These data replicate and extend previous results that used a different route of administration (intravenous), a different species (rhesus macaque), and a different BChE product (non-CGMP material). The addition of two sensitive neurobehavioral tests coupled with the PK/PD results convincingly demonstrates the neurobehavioral safety of plasma-derived Hu BChE at therapeutic levels. Protection against an otherwise-lethal dose of soman by a pre-exposure treatment dose that is devoid of side effects establishes a foundation for additional testing using other exposure routes and treatment times, other challenge agents/routes, or other classes of organophosphate scavengers.

Acknowledgement and disclaimers

Opinions, interpretations, conclusions, and recommendations are those of the author(s) and are not necessarily endorsed by the US Army.

This research complied with the Animal Welfare Act and implementing Animal Welfare Regulations and adhered to the principles noted in The Guide for the Care and Use of Laboratory Animals.

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