Solithromycin for the Treatment of Anthrax

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Background: Solithromycin, a fourth generation macrolide, is in Phase 3 clinical trials for community-acquired bacterial pneumonia (CABP) and is being developed for both oral and intravenous administration for treatment of hospital-acquired bacterial pneumonia (HAP), ventilator-associated bacterial pneumonia (VABP) and invasive bacterial pneumonia (IBP). Solithromycin, an oral macrolide antibiotic, has demonstrated broad activity against Gram-positive and Gram-negative bacteria, as well as anaerobic bacteria. Initial studies with solithromycin suggested that it has an advantage over other macrolides in that it is active against macrolide-resistant bacteria. The oral agent has a high bioavailability ranging from 50% to 70% of the administered dose, which has enabled the development of a once-daily oral dosage regimen for the treatment of CABP. Further, solithromycin has demonstrated favorable pharmacokinetics, with rapid absorption and high oral bioavailability, which are critical for effective treatment of infections that require rapid action.

Methods: This study evaluated the efficacy of solithromycin against a strain of Bacillus anthracis spore in cynomolgus macaques (CMs). A randomized, split-dose protocol was used to evaluate the efficacy of a single dose of solithromycin in CMs, followed by a second dose administered intravenously (IV). The study was conducted in two phases. In the first phase, CMs were randomized into two groups: a solithromycin group and a vehicle control group. In the second phase, the CMs in the solithromycin group were randomized into two subgroups: one subgroup received the second dose of solithromycin by oral gavage (SID) and the other subgroup received the second dose of solithromycin by IV. The study was conducted in accordance with the guidelines of the Institutional Animal Care and Use Committee (IACUC) of the University of Texas at Austin.

Results: All CMs in the solithromycin group survived the challenge with Bacillus anthracis, whereas two CMs in the vehicle control group died. The overall survival rate in the solithromycin group was 100%, while in the vehicle control group it was 50%. The time to death for the non-survivors in the vehicle control group was 12-14 days. The level of protective antigen (PA) was measured using a PA enzyme-linked immunosorbent assay (ELISA) at the time of death. The levels of PA were significantly lower in the solithromycin group compared to the vehicle control group.

Conclusions: Solithromycin is an effective and safe treatment for anthrax in non-human primates. Further studies are needed to determine the minimal dose and duration of treatment necessary to treat anthrax.