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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 (IV) use. Through an ongoing partnership with BARDA, Cempra is developing SOLI for use in pediatrics, and has evaluated SOLI for use against bioterror threat pathogens. This study evaluated the therapeutic efficacy of solithromycin against a lethal inhalational challenge with *Bacillus anthracis* spores in cynomolgus macaques (CM).

**Methods:** CMs were challenged with a target dose of 200 *B. anthracis* (Ames strain) LD50 equivalents via aerosol exposure. Solithromycin or vehicle treatment (oral gavage) was initiated on an individual basis following detection of circulating protective antigen and administered once daily for 21 consecutive days. Solithromycin-treated animals were administered a humanized dosing regimen designed to mimic human exposures achieved with the oral CABP regimen (800 mg loading dose, 400 mg maintenance dose). Animals were observed for 36-37 days post-challenge (14 days post-last treatment) and evaluated by blood culture, PA-ECL, body temperature, toxin neutralizing antibody (TNA) and anti-PA IgG ELISA, assessment of bacterial load in the tissues, and histopathology.

**Results:** All CMs were confirmed bacteremic prior to treatment. All vehicle control-treated animals (7/7) succumbed following aerosol exposure to *B. anthracis*, while survival in the solithromycin group was 83% (10/12). Elevated body temperatures of solithromycin group survivors resolved to baseline levels by Days 4-5 post-challenge. Samples of the liver, brain, spleen, and mesenteric lymph node from all surviving solithromycin-treated animals were negative for *B. anthracis*. Bacteria consistent with *B. anthracis* was observed for 60% (6/10) or 20% (2/10) of the surviving solithromycin-treated animals in the samples of the lung and tracheobronchial lymph node, respectively, but the levels were below the limit of quantitation for all of these animals. By the end of the study (14 days post-last treatment), all survivors had developed positive anti-PA IgG and TNA titers, indicative of an immunologic response in the surviving animals.

**Conclusion:** Solithromycin is efficacious in the CM pulmonary anthrax therapeutic model.