

## **Treatment of Normal and Immune Suppressed Cotton Rats with IVIG Containing High Neutralizing Titer Anti-RSV Antibody**

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**Background:** Respiratory syncytial virus (RSV) is recognized as a significant problem in both pediatric and adult immunocompromised hosts and is associated with significant morbidity and mortality. The severity of clinical manifestations and the incidence of mortality depends on the magnitude of the immune suppression. The group at highest risk for severe RSV infection is bone marrow transplant recipients. We have previously demonstrated that our product, RI-002 which is an IVIG containing standardized, high levels of neutralizing anti-RSV antibody titers prevents pulmonary infection in a cotton rat model of RSV, an animal model regarded as the ideal surrogate for RSV infection in humans. RI-002 is currently fully enrolled in a phase three clinical trial designed to prevent serious infections in patients with primary immune deficiency disease (PIDD). This study in the cotton rat was designed to determine whether RI-002 could treat normal and immune suppressed RSV infected animals.

**Methods:** Cotton rats chronically suppressed with Cytoxan showed a 90% reduction of lymphocytes and circulating immune globulin. Animals were challenged with  $5 \times 10^7$  RSV/A/ long and injected intraperitoneally on day 1 (normal animals) and days 1, 4 and 7 (immune suppressed animals) with RI-002 and sacrificed on day 10. Results: There was a 99.9% (3 log) reduction in viral load in both lung and nasal tissue of normal and immune suppressed cotton rats with the reduction being slightly greater in the tissues of normal animals. Histopathology of the lungs in the immune suppressed cotton rats showed perivascular, interstitial and alveolar inflammation and epithelial death with significant improvement in all of these parameters in the animals treated with RI-002. Strikingly, in the peripheral organs of immune suppressed animals there was evidence of systemic dissemination of the virus by PCR and this was reduced after treatment with RI-002.

**Conclusions:** IVIG containing standardized, high levels of neutralizing RSV antibody titers may be an effective treatment to suppress both RSV induced viral load and viral induced inflammation in the lungs, as well as to suppress systemic dissemination of the RSV virus.