**Use of High Titer RSV Immunoglobulin (RI-001-RSV IVIG) in Immunocompromised Adults**

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**Abstract**

Background: Respiratory Syncytial Virus (RSV) causes fatal respiratory tract infection in immunocompromised patients. Infusion of immunoglobulin (IG) with high levels of neutralizing RSV antibody (RSV-IVIG) may offer therapeutic benefit in immunocompromised populations.

Methods: Compassionate use of RSV-IVIG (RI-001-RSV IVIG, ADMA Biologics) was allowed in 3 immunocompromised patients from the US (2 allo-HSCT and one CLL) and 4 from Australia with documented RSV lower respiratory tract infection. RSV-IVIG was administered at 1500mg/kg on day 1 and 750mg/kg on day 3. Patients were treated with corticosteroids. Patients 1-3 received standard HSCT IG and were neutropenic. Patient 4 received standard HSCT IG and was not neutropenic. None developed bronchiolitis or pneumonitis. RSV Ig was quantified in respiratory secretions of the patient with CLL.

Results: RSV-IVIG was well tolerated and had no serious side effects. All recovered and all food - 4 fold or greater increase in RSV neutralizing antibody. The patient with CLL had no measurable antibody pre-infusion and a GMT of 7708 after the second infusion. Associated with the rise in antibody was a 22 fold drop in viral RNA on day 3. No patient had clinical or radiographic pneumonitis or bronchiolitis.

Conclusion: Administration of high titer RSV immunoglobulin was associated with an increase in serum neutralizing antibodies in severe immunocompromised adults with RSV lower respiratory tract infections. Future studies are needed to determine efficacy.

**Compassionate Use RI-001**: The safety and efficacy of RI-001 is presently being evaluated in a clinical trial of pediatric patients with documented RSV lower respiratory tract infections who are at risk for progression to lower tract disease (RSV-001). Patients with URI at presentation were excluded from the study but eligible for compassionate use of the product on a case by case basis with application to the FDA for emergency IND. Seven patients received compassionate use treatment. RSV-IVIG was administered at 1500mg/kg on day 1 and 750mg/kg on day 3. Serum was collected pre and post infusion on days 1 and 3, and as well as day 8, 10, 12, 16 and 33. Four of seven patients also received standard IG.

Serum levels of RSV were measured with a standard amount of Al (A stress) RSV for 30 minutes in culture plates. IgG2 cells were then added to the wells and the plates incubated at 37°C in CO2 for 3 days. The plates were fixed and RSV antigen quantified by ELISA using an RSV neutralizing antibody. The neutralization titre was defined as the titre of serum that reduces color development by 50%.

**Case Report - Subject 3**: This patient is an 84 year old with CLL, undergoing intensive chemotherapy. On day 44 the patient developed bronchiolitis. The patient initially presented with nasal and retinal symptoms which slowly resolved but he developed progressive dyspnea and a productive cough after 18 days of illness. Chest X-ray showed diffuse interstitial infiltrates. The worst onset of interstitial infiltrates was on day 44. On day 44 the patient received RSV-IVIG at 1500mg/kg on day 1 and 750mg/kg on day 3. By day 4 the breathing had resolved and he was feeling much improved. Oxygen saturation improved and it was discontinued on day 5. The patient was in clinic on day 44, and his RSV-IVIG was not depleted. The patient was discharged on day 33 with no evidence of RSV-IVIG depletion. The patient then received RSV-IVIG over time and became negative on 5/1. The patient began chemotherapy for his CLL, the week of 5/17 and had no recurrence of RSV.