When immunocompetent individuals contract RSV infections the vast majority are confined to the upper respiratory tract and resolve without sequelae. In contrast, immunocompromised patients are at high risk of having lower respiratory tract infections (LUI) progress to lower respiratory tract infection (LRTI). Both solid organ transplant patients and allogenic bone marrow recipients are particularly susceptible to developing RSV infections within the first few weeks post-transplantation. There are currently no RSV approved therapies for the treatment of RSV infections in immunocompromised transplant patients. The reported mortality rate in bone marrow transplant patients who develop lower respiratory tract infections approaches 40% for those not treated or treated late with standard of care therapy. A safe and effective alternative treatment that will reduce and/or eliminate RSV LRTI in these critically-ill patients, and ADSMA Biologies IVIG is a newly developed human immunoglobulin product supplied as a 10% solution for intravenous use. RSV not uncommonly infects immunocompromised individuals and can progress to severe lower respiratory tract disease unresponsive to conventional therapy. From April 2009 through February 2011, 15 unsolicited compassionate use requests (EIND) were received for ADMA IVIG in patients with progressive RSV disease unresponsive to conventional therapy. From April 2009 through February 2011, 15 unsolicited compassionate use requests (EIND) were received for ADMA IVIG in patients with progressive RSV disease unresponsive to conventional therapy.

PHASE II MULTICENTER DOSE RANGING STUDY IN RSV INFECTED IMMUNOCOMPROMISED PATIENTS

STUDY DESIGN:
- Randomized, double-blind, placebo-controlled
- 4 centers in the United States
- EXP by IFN or placebo at enrollment
- RSV by RT-PCR at enrollment
- 87 patients randomized
- 2 years of concurrent immunosuppressive treatment
- Assess AEs (1-60 months)
- Three Arms: 1-1-1
- 1 arm treated with 500 mg/kg day 2
- 2 arms treated with standard care
- Three Arm: 1-1-1
- 1 arm treated with 500 mg/kg day 2
- 2 arms treated with standard care

PHASE II PRIMARY OUTCOME

Primary Endpoint
- Define the dose which produced a >4-fold increase in neutralizing titer at day 18 compared to baseline
- Secondary endpoints
- Well tolerated, no SAEs related to study drug

DOSE

<table>
<thead>
<tr>
<th>Group</th>
<th>Placebo</th>
<th>500 mg/kg</th>
<th>750 mg/kg</th>
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<tbody>
<tr>
<td>A</td>
<td>25</td>
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Note: Data for 500 mg/kg was not available at day 18 with 750 mg/kg.

COMPREHENSIVE USE EXPERIENCE

- 40 unsolicited compassionate use requests (EIND)
- Age 3 months-71 years
- All patients were immune suppressed and diagnosed with RSV lower respiratory tract infection
- All patients were unresponsive to conventional standard of care therapies
- Some had received Ribavirin and/or Standard IVIG
- 3 young children received palivizumab
- 3 patients treated with Ribavirin and/or Standard IVIG
- 3 patients treated with Ribavirin and/or Standard IVIG
- 3 patients treated with Ribavirin and/or Standard IVIG
- 3 patients treated with Ribavirin and/or Standard IVIG

VIGNETTES FROM COMPASSIONATE USE EXPERIENCE

Patient #1
- 59 yo male post HTX transplant
- 2 weeks PFT PA improvement
- CXR RUL consolidation
- RSV- (LRU)
- Failed conventional therapy
- ADMA IVIG administered day 1 day 2 for RSV diagnosis. Patient clinically and symptomatically improved by 2 days

Patient #2
- 45 yo male with CLL
- 12 days PFT URI. left, SOB
- CXR diffuse bronchitis
- RSV+ (LRU)
- Failed conventional therapy
- ADMA IVIG administered day 2 after RSV diagnosis. Patient clinically and symptomatically improved by 3 days

Patient #3
- 2 yo female post HTX transplant
- 3 days PFT cough. mood, confusion. increasing SOB
- CXR RUL consolidation
- RSV+ (LRU)
- Failed conventional therapy
- ADMA IVIG administered day 1 after RSV diagnosis. Patient clinically and symptomatically improved by 1 days

Patient #4
- 49 yo male with ALL treated SCT 10 months PTA
- Increasing respiratory rate 28/min and increasing CXR
- CXR diffuse plague congestion in middle and lower lobe bifurcation
- RSV+ (LRU)
- Failed conventional therapy
- ADMA IVIG administered day 4 after RSV diagnosis. Patient clinically and symptomatically improved by 2 days

SUMMARY OF ANIMAL AND HUMAN STUDIES

- ADMA Biologies IVIG contains standardized, high levels of neutralizing titers to RSV
- Prevents RSV URI and RSV LRI in immunocompetent and immune suppressed cotton rats
- When infused into RSV infected human immune competent subjects, there is a greater than or equal to 4-fold increase in RSV neutralizing titers in the serum
- When evaluated in 15 compassionate use patients with RSV lower tract disease and progressive respiratory distress which was refractory to conventional treatment, administration of ADMA IVIG was associated with favorable outcomes in 13 out of 15 patients
- The above data suggests that this RSV high titer immune globulin product may be a useful adjunct for the treatment of RSV lower tract disease in the solid organ, and bone marrow transplant population

POLYCLONAL HUMAN INTRAVENOUS IMMUNE GLOBULIN (IGIV) WITH HIGH LEVELS OF RSV NEUTRALIZING ANTIBODIES: A SUMMARY OF ANIMAL AND HUMAN STUDIES

Respiratory syncytial virus (RSV) is a common cause of respiratory infection in children and adults. Despite the lack of specific antiviral therapy, RSV infection affects immunocompetent individuals and can progress from upper respiratory tract disease (URTI) to RSV lower respiratory tract disease (LRTI). Effective antiviral agents are not available and current treatment options limited. To determine whether high titer neutralizing antibody to RSV might be effective in the treatment of RSV infection, we prepared a plasma-derived, human polyvalent immunoglobulin globulin using plasma obtained from donors treated for the purpose of high levels of neutralizing titers to RSV. To ascertain whether this polyclonal RSV enriched pool of antibodies translated into in vivo efficacy we studied its ability to prevent infection in cotton rats infected with RSV. Animals were infected with the intranasal route, and controls were infected intranasally with RSV using 105 PFU per gram of tissue. The majority of animals treated with saline had mean titers of >4.0 Log10 PFU/g of tissue in the lung and the experimental groups given 150, 750, and 1500 mg/kg had undetectable RSV viral titers in the lungs of all animals. The mean nasal titers were ~5 Log10 PFU/g of tissue in the lungs and the experimental groups given 150, 750, and 1500 mg/kg had undetectable RSV viral titers in the lungs of all animals. The mean nasal titers were ~5 Log10 PFU/g of tissue in the lungs and the experimental groups given 150, 750, and 1500 mg/kg had undetectable RSV viral titers in the lungs of all animals.

ADMA IVIG PREVENTS RSV INFECTION IN THE LUNG OF IMMUNE COMPETENT COTTON RATS

WHOLE BLOOD ANALYSIS DATA IMMUNE SUPPRESSED COTTON RATS

SERUM TOTAL IgG IMMUNE SUPPRESSED COTTON RATS

POLYCLONAL HUMAN INTRAVENOUS IMMUNE GLOBULIN (IGIV) WITH HIGH LEVELS OF RSV NEUTRALIZING ANTIBODIES: A SUMMARY OF ANIMAL AND HUMAN STUDIES

Ann R. Falsrey, Edward W. Walsh, University Of Rochester School Of Medicine, Rochester N.Y.
James J. Mond, ADMA Biologics, Ramsey NJ