Compassionate Use Experience with High Titer RSV Immunoglobulin (RSV-IVIG) in RSV Infected Immunocompromised Persons


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**Conflict of Interest: Dr. Bates is a consultant for Innate Immunotherapeutics, Inc. Innate Immunotherapeutics, Inc. is the developer of the intravenous immunoglobulin provided to patients in this compassionate use study.

**Introduction

Respiratory syncytial virus (RSV) may cause severe disease in persons with compromised immune function. Recipients of chimeric hematopoietic cell transplant (CHCT) and/or patients with chronic graft versus host disease may be particularly high risk for severe infection. Optimal therapy for immunocompromised patients with RSV infection has not been defined. Ribavirin has been used as a single agent to treat RSV infection in immunocompromised patients with RSV, despite variable efficacy. A recent phase II trial of the monoclonal antibody, palivizumab, in immunoglobulins, generally combined with ribavirin. There are also two intravenous immunoglobulin products, palivizumab and pooled human intravenous immunoglobulin (IVIG) discussed in this report. Palivizumab is a recombinant IgG antibody, whereas intravenous immunoglobulin is a mixture of polyclonal antibodies. Palivizumab is generally given orally, or when intravenous immunoglobulin is not readily available. The results of a compassionate use study in patients with severe RSV disease who failed conventional treatment were very high for progression of RSV infection.

**Method

**Patients

Data were collected from patients who received intravenous immunoglobulin (IVIG). In the United Kingdom, to date, there have been no compassionate use studies with high titer RSV immunoglobulin (RSV-IVIG) in RSV infected immunocompromised persons. The data in this report were collected in Europe from patients with severe RSV disease who had not responded to conventional therapy. The patients were 14 patients who received compassionate use RSV-IVIG in Europe from December 2008 to February 2011. All patients had a documented RSV infection at diagnosis. Thirteen patients received RSV-IVIG between days 1 and 5 of illness after RI-001. One patient received RI-001 at day 15 of illness after RI-001.

**Study Population

The study was conducted to determine the safety and efficacy of high titer RSV immunoglobulin in severe RSV infection in immunocompromised persons. This study was a multicenter, open label, Phase II study of RSV-IVIG. Participants were randomized to either the RSV-IVIG arm or the control arm. The primary endpoint was survival at 21 days after initiation of the study. The secondary endpoints were pulmonary and systemic outcomes.

**Results

Ten patients were treated with RI-001 (333 mg/kg on days 1, 3, 5, and 7). Seven patients were treated with RI-001 (333 mg/kg on days 1, 3, 5, and 7) and palivizumab (15 mg/kg on days 1, 15, and 29). Pulmonary outcomes were measured by chest radiographs (CXR) and/or computerized tomography (CT). Twenty-nine patients were treated with RI-001 (333 mg/kg on days 1, 3, 5, and 7). The CXR and CT findings were consistent with severe respiratory disease. The CXR and CT findings were consistent with severe respiratory disease for patients treated with RI-001. All patients had at least one CXR or CT performed.

**Discussion

The results of the compassionate use experience with high titer RSV immunoglobulin (RSV-IVIG) in RSV infected immunocompromised persons indicate that high titer RSV immunoglobulin (RSV-IVIG) may be effective in treating severe RSV infection. The safety and efficacy of high titer RSV immunoglobulin (RSV-IVIG) in severe RSV infection in immunocompromised persons require further study.

**Conclusions

• RSV-IVIG infusions were safe and well tolerated with minimal side effects.
• Administration of RSV-IVIG resulted in significantly higher levels of neutralizing antibody against RSV.
• These results suggest that early treatment with RSV-IVIG improves survival in patients with RSV LRTI.