Treatment of RSV Lower Respiratory Tract Infection in Two Immunocompromised Children with Polyclonal Immunoglobulin Containing Standardized Levels of Neutralizing Anti-RSV Antibodies

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Background

- Respiratory syncytial virus (RSV) can cause severe lower respiratory tract infection (LRTI) in immunocompromised patients. [1,2]
- No standard, effective therapy for severe RSV LRTI currently exists.
- Use of ribavirin (inhaled or oral), pooled donor intravenous immunoglobulin (IVIG), and monoclonal anti-RSV antibodies (palivizumab) have been described. [1]
- RI-002 (ADMA Biologics) is a pooled human polyclonal IVIG containing standardized levels of neutralizing anti-RSV antibodies that is prepared via a patented process. [2,3]
- The predecessor of RI-002 was used for compassionate treatment in RSV LRTI in stem cell transplant patients. [2,3]
- RI-002 was FDA-approved in 2019 for prophylaxis in primary immunodeficiency patients.

Methods

- Two children with T-cell lymphoblastic lymphoma and neutropenia secondary to chemotherapy were included
- Both patients had RSV LRTI
- Both received PO ribavirin and IVIG
- Both were treated with RI-002 under an emergency FDA Investigational New Drug application

RI-002 [3,4]

Table 2. Comparison of respiratory virus titers of RI-002 and commercial IVIG batches [11].

Virus	Ratio of geometric means (95% CI) (RI-002/commercial IVIG)[a]	p-Value[b]
RSV	1.863 (1.249, 2.771)	0.003
PIV 1	1.792 (1.282, 2.505)	0.001
OC43	1.610 (1.127, 2.301)	0.010
PIV 2	1.601 (1.160,2.210)	0.005
229E	1.494 (1.144, 1.950)	0.004
Flu A	1.402 (1.067, 1.843)	0.016
Flu B	1.316 (1.026, 1.688)	0.031
hMPV	1.264 (0.990, 1.613)	0.060
PIV 1 and 2	1.694 (1.250, 2.296)	0.001
OC43 and 229E	1.551 (1.237, 1.945)	<0.001
All viruses[c]	1.529 (1.227, 1.907)	<0.001

[3]Wasserman RL et al. 2017. PMID: 29035131

- Pooled polyclonal intravenous immune globulin with standardized levels of neutralizing anti-RSV antibodies
- Derived from human plasma donors tested to have high levels of neutralizing antibodies to RSV

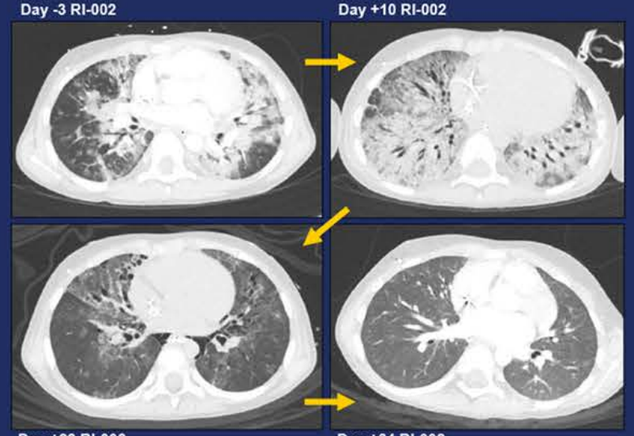
Patient #1: Clinical Course

- Admitted (Hospital Day [HD] #1) with fever, neutropenia, and nasal congestion; NP RSV PCR positive
- HD#9-17: Progressive respiratory failure
- HD#17: Intubated for respiratory failure. Initiated on ribavirin PO 30 mg/kg/day, received 0.5 g/kg IVIG and palivizumab
- HD#18: High frequency oscillation, paralysis, and nitric oxide. Mediastinal air leak. Emergent IND FDA approval for RI-002
- HD#20: RI-002 1st Dose (1.5 g/kg)
- HD#22: RI-002 2nd Dose (0.75 g/kg)
- HD#23: Progressive air leak, elective V-V ECMO
- HD#30: Chest CT severe ground glass opacities with new diffuse bronchiectasis; down-trending crossing point (Cp) values
- HD#34: RI-002 3rd Dose (0.75 g/kg)
- HD#38-42: Improved pulmonary compliance, negative ETT RSV PCR so ribavirin discontinued; on dexamethasone; Tracheostomy HD#43
- HD#52: V-V ECMO discontinued, weaning respiratory support

Discharged home HD#88

1 month later returned for tracheostomy de-cannulation, currently at respiratory baseline with no support

Patient 1: Serial CT images at level of left atrium while on RI-002



Patient #1 Microbiology Data

Hospital Day (HD)	RI-002 treatment	Specimen type	RSV PCR Result	RSV PCR Cp*	Viral Culture
HD5		NP swab	Positive	n/a	n/a
HD10		BAL	Positive	21.1	RSV positive
HD17		BAL	Positive	23.2	RSV positive
HD20	1.5g/kg				
HD22	0.75g/kg				
HD24		BAL	Positive	29	No growth
HD29		NP swab	Negative	n/a	n/a
HD29		ETT aspirate	Positive	33.8	No growth
HD33		ETT aspirate	Positive	35.7	No growth
HD34	0.75g/kg				
HD36		ETT aspirate	Negative	n/a	No growth
HD37		NP swab	Negative	n/a	n/a

*PCR Cp values are a semi-quantitative determination of strength of positivity
NP, nasopharyngeal; BAL, bronchoalveolar lavage;
ETT, endotracheal; n/a, not available; Cp, crossing point

Patient #2: Clinical Course

- Admitted (HD#1) with fever, neutropenia, nasal congestion, cough, and stridor; NP RSV PCR positive
- HD#1: 1L NC (2/19)
- HD#2-3: IVIG 0.5 g/kg + Oral ribavirin 30 mg/kg/day
- HD#4: Dexamethasone x 3 days for stridor
- HD#5: RI-002 (1.5 g/kg)
- HD#6: Off oxygen, afebrile
- HD#7: RI-002 (0.75g/kg), ribavirin discontinued

Discharged home HD#8

Conclusions

- Polyclonal immunoglobulin (RI-002) contains high levels of neutralizing anti-RSV antibodies.
- In immunocompromised children:
  - RI-002 may be useful in the treatment of severe RSV LRTI.
  - RI-002 may be useful in preventing RSV infection or its progression to severe LRTI.
- Future studies on the role of RI-002 in the treatment and prevention of RSV LRTI in immunocompromised children are warranted.

References

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