Prospective Observational Study in Japanese Children Hospitalized with Respiratory Syncytial Virus Related Lower Respiratory Tract Infections

Respiratory Syncytial Virus (RSV) is one of the leading causes of acute respiratory infections, frequently requiring hospitalization. Various supportive care measures have largely failed to demonstrate clinically significant benefit in reducing disease burden. Recent antiviral trials in adults demonstrate promising effects on viral kinetics and symptomatology. Data in young children for daily viral shedding and changes in clinical symptoms during the hospitalization is still limited worldwide and requested to position the clinical development of RSV intervention strategies. Our objective was to assess in hospitalized children, the rate of RSV viral clearance in nasal specimens and clinical symptoms kinetics, based on daily sample collection and clinical monitoring.

**Study Design**
- Multicenter, prospective observational study
- Study period: Dec 2013 - Jan 2015
- Target Number: 50 (with at least 3 days swabs)

**Inclusion criteria**
1. Aged 5 years or younger
2. RSV positive with rapid antigen detection kit
3. Hospitalized with LRTI
4. ≤ 5 days from clinical onset
5. Informed consent obtained within 24h from admission

**Endpoint**
- RS viral load (nasal swab)
- Clinical symptoms score
- Medical support score

**Observation period**
- Day 0 or discharge, whichever comes first
- No restriction for Standard of Care

**PROCEDURE**
- Daily nasal swabs were collected from the mid-turbinate region and stored in universal transport media at minus 20 degrees Celsius. Swabs were sent to Catholic University of Leuven, Belgium for transcriptase polymerase chain reaction.

**Viral load change from day 1 to 3 (based on day of assessment) did not correlate with the length of oxygen supplementation, CSS, and MSS.**

**Children older than 12 months of age were more likely to have underlying disease (58.8% vs 9.3%), with delayed time to peak VL (2 vs 1 days), and lower VL (∆0.3 vs 1.1 log), longer request for oxygen supplementation and higher median viral load at discharge (6.8 vs 6.2 log), compared to children without underlying disease.**

**The confounding impact of age, underlying diseases, and corticosteroid use could not be differentiated in the current analysis.**

**Conclusion**
- In a cohort of children hospitalized for RSV disease, those with underlying disease were more represented in the older age group (12+ months), had delayed RSV viral load peak and longer request for supplemental oxygen.

**Key findings and discussion**
- Viral load and CSS gradually decreased in parallel after hospitalization.
- Viral load change from day 1 to 3 (based on day of assessment) did not correlate with the length of oxygen supplementation, CSS, and MSS.
- Viral load kinetics and CSS did not differ according to RSV subtype (data not shown).
- Children younger than 12 months of age were more likely to have underlying disease (58.8% vs 9.3%), with delayed time to peak VL (2 vs 1 days), and lower ∆VL of log VL (0.3 vs 1.2 log), compared to children 12 months of age or younger.
- Children with underlying disease had a delayed time to peak VL (2.5 vs 2 days), lower ∆VL of log VL (0.3 vs 1.1 log), longer request for oxygen supplementation and higher median viral load at discharge (6.8 vs 6.2 log), compared to children without underlying disease.
- 14 patients, mainly in the oldest age group, had underlying asthma or reactive airway disease and received systemic corticosteroids. There was delayed time to peak in viral kinetics in patients receiving corticosteroid treatment.
- The confounding impact of age, underlying diseases, and corticosteroid use could not be differentiated in the current analysis. Given the delayed peak in viral load and prolonged symptoms, this subset of patients may be a target for antiviral intervention in the future.

**Disclosures**
This study was conducted under a grant from Janssen Pharmaceuticals awarded to IM and MS. IM, MS, NS have served as a scientific advisors of Janssen Pharmaceuticals. Data analysis was performed by Janssen Pharmaceuticals. The study was approved by the institutional review board at the National Center for Child Health and Development and Keio University School of Medicine.