Reviewer's report

Title: Association of RSV-Related Hospitalization and Non-compliance with Palivizumab among Commercially Insured Infants: A Retrospective Claims Analysis

Version: 1 Date: 5 May 2013

Reviewer: James Nokes

Reviewer's report:

Major compulsory

1. Methods. Study sample. Page 4. “The first was the post-index period, defined as the index date through April 30 of the following year.”

I am concerned about this post-index observation period. Between compliant and non-compliant there may be a difference in the cumulative RSV exposure time since compliant individuals are likely to have begun prophylaxis earlier than non-compliant, hence the observation time at risk for compliant individuals could be diluted by early low exposure. Non-compliant infants who start prophylaxis on average later will thus be exposed to higher rates of RSV transmission. What was the average duration of pre-RSV exposure by compliance group?

2. Methods. Outcome measures. Page 5. “The major outcome of interest was RSV-related hospitalizations, identified using RSV-specific diagnosis codes (079.6, 466.11, 480.1) and RSV-like diagnosis codes…”

This represents a risk of mis-classification since actual RSV infection could not be assured. What is the likelihood of these RSV-like diagnoses not being RSV, and might they differ between compliant and non-compliant? What effect would it have on the results to remove the RSV-like diagnoses from the multivariate analysis?

3. Results. RSV-related Outcomes by Compliance Status. Page 8. “Twenty-seven percent [61] of all RSV-related hospitalizations captured in the study occurred prior to the index dose of palivizumab. The non-compliant group had a larger proportion of hospitalizations prior to the index dose than the compliant group (24.9% vs. 2.2% of RSV-related hospitalizations, respectively)..”

Should these 61 children be in the study? The study is trying to show the difference between non-compliance and full compliance while taking prophylaxis. But in the case of these 61, they were not started on prophylaxis when infected. We know Palivizumab works, so if the results are reliant on these 61 being included then is the study telling us anything new?

What is result of changing the inclusion criterion to only include infants who received a first dose before the RSV season?
Minor essential


Why was the study between 2003 and 2009. Why not up to 2012 for instance?

5. Methods. Outcome measures. Page 5. “To control for variable pre-index and post-index periods, all healthcare utilization was calculated per subject per month.”

Could you explain how this measure controls for the variable periods?

6. Methods. Multi-variate analysis. Page 6. “To understand the stability of the results, the final model was run in population subsets to measure the relationship between non-compliance and RSV-related hospitalizations in specific population cohorts. “

Please clarify what is being undertaken and why.

7. Results. “Figure 2. Timing of First Palivizumab Dose by Compliance Status”

Graph does not make sense. What is the Y axis describing as proportions go above 1? Title here does not seem to relate to figure.

8. Results Palivizumab utilisation. Page 7. “Eighty-seven percent of the index palivizumab doses were given in October (58.7%) or November (28.2%) (Figure 2).”

The figure 2 content does not relate to this text.

Discretionary revisions

9. Methods. Study sample. Page 4. “To ensure the ability to clearly identify all doses, infants born between October 1 and April 30 were excluded from the study.”

It would be useful to include more explanation in the text on the reason why these infants born between Oct 1 and April 30 were excluded.

10. Results. Table 1. Twins and multiple births of >30%

The proportion of multiparous pregnancies seems very high. Is this unusually high?

11. Results Palivizumab utilisation. Page 7. “Overall, 75% of subjects received at least 5 palivizumab doses”

One study objective could be to see if there is a difference in protection between regular on time dosing and non-regular in those who receive >=5 doses. This analysis would exclude (i) those infected before first dose and (ii) those <5
doses.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests