Author’s response to reviews

Title: Duration of viral shedding in hospitalized patients infected with pandemic H1N1

Authors:

Silvia Meschi (silvia.meschi@inmi.it)
Marina Selleri (marina.selleri@inmi.it)
Eleonora Lalle (eleonora.lalle@inmi.it)
Licia Bordi (licia.bordi@inmi.it)
Maria B Valli (mariabeatrice.valli@inmi.it)
Federica Ferraro (federica.ferraro@inmi.it)
Giuseppe Ippolito (giuseppe.ippolito@inmi.it)
Nicola Petrosillo (nicola.petrosillo@inmi.it)
Francesco N Lauria (francesco.lauria@inmi.it)
Maria R Capobianchi (maria.capobianchi@inmi.it)

Version: 5 Date: 23 February 2011

Author’s response to reviews: see over
Dear Editor, we are resubmitting our paper entitled:

RE: manuscript: MS: 1195715970434904

Title: DURATION OF VIRAL SHEDDING IN HOSPITALIZED PATIENTS INFECTED WITH PANDEMIC H1N1

All the requested changes (in underlined text) have been performed, and the points raised by the reviewers have been addressed.

The point by point answer is as follows:

**Associate Editor's comments:**

- Minor essential revisions:
  The following grammatical changes should be made prior to publication.

ANSWER:
All requested grammatical changes have been made.

**Referee 1 Comments (Wilina Lim):**

Minor essential revisions are required as follows:

- Page 10, line 7 – 10, the number of patients on antiviral treatment did not add up. The authors stated there were 29 patients on antiviral, but only 24 + 4 were described.

ANSWER:
We agree and the mistake has been amended; in fact, the patients treated with oral oseltamivir at standard dosage were 25 (86.2%) (Page 10, line 9).

- Page 10, line 8, there was a typo (75mg two twice/day).
- Page 14, line 23, “H175Y” should be “H275Y”.

ANSWER:
We corrected the typos.

- Page 12, line 8, “presence of any complication” needs to be appropriately defined or described.

ANSWER:
The complications mentioned at page 12, line 8 were listed (already in the previous version) in the table 2, footnote d (Page 25). Now we have added the list of complications also in the text (Page 12, lines 8-9).
Referee 2 Comments (Edward Goldstein):

Minor essential revision:

- The reviewer’s remaining concern is that it appears from looking at Figure 2 A and 2C that pneumonia is negatively associated with receipt of antivirals. If this is so, the results in Figure 2B and 2C may be biased.

ANSWER:

We agree that Fig. 2A and 2C may generate the idea that pneumonia is negatively associated with receipt of antivirals; however this is not the case, as 10/11 pneumonia patients (90.9%) received antiviral treatment. We added a statement to make more clear cut this situation (Page 10, line 18).

- Is it possible to examine the effect of one of the variables (pneumonia and (early) antivirals) adjusting for the other? For example, one can do logistic regression where the outcome is PCR detection on days 6-7 (or 8-9) and the variables are pneumonia and antiviral treatment (the former presumably is significant). Similarly one can do logistic regression where the outcome is Log viral load over 4.5 (or 4.6) on days 4-5 with the same variables.

ANSWER:

We agree that logistic regression analysis is the best way to identify the contribution of individual factors to the prolonged shedding. However, because of limited number of cases, it was not possible to apply multivariate analysis to this study, as already mentioned in the paper. A statement has been added, to further underline this point at page 14 (lines 14-16). The small numbers is in fact a limitation of the present study, and we further acknowledge this limitation at page 16 (lines 4-6).
Referee 3 Comments (Michael Ison):

- The paper does not add significantly to the available literature although does have some findings that are somewhat discrepant with other reports.

ANSWER:
We agree that our results are in line with literature data, but are somewhat discrepant with other reports. We further underlined such discrepancies in the discussion (Page 13 lines 20 onwards).

- The available data are limited which in turn limits the utility of the findings (i.e. only a small subset of patients had serial testing for resistance...).

ANSWER:
We are aware that our study has some limitations, that, unfortunately, could not be overcome, mainly due to the small numbers of analyzed patients and to the retrospective nature of the study. We further remarked these limitations in the Discussion (Page 16, lines 3 onwards); in addition, we reinforced the statement that the sequence analysis of viral strains was only performed in the patients with sufficient left sample volume (Page 12, lines 16-18).

- Quality of written English: Needs some language corrections before being published.

ANSWER:
Language corrections were included to improve the quality of written English.