Reviewer's report

Title: Seroconversion and asymptomatic infections during oseltamivir prophylaxis against Influenza A H1N1 2009

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Reviewer: Pedro A Piedra

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This manuscript reports on an observational cohort study that evaluated the serologic outcome during oseltamivir prophylaxis and after post-exposure prophylaxis during three nH1N1 outbreaks in the Singapore military. The three outbreaks involved a total of 252 subjects. A strategy of oseltamivir chemoprophylaxis with cohorting of the affected unit was used to limit the spread of the nH1N1 virus. A 10 day course of oseltamivir prophylaxis was administered at the onset of the outbreak. NP swabs were collected 3 times per week and tested for nH1N1 by RT-PCR. Screening was maintained until no new cases were identified for three days. All subjects positive for nH1N1 by RT-PCR were given a minimum of a 7 day home medical leave. Also up to three blood samples for HI tests were collected at start of the outbreak, 2-3 weeks after completion of chemoprophylaxis and 4-6 weeks after completion of chemoprophylaxis. The last blood sample was obtained after the peak of nH1N1 activity in Singapore. There were 11 index cases, 16 subjects who developed >4 fold-rise in HI between 1st and 2nd blood samples and 23 subjects who seroconverted between the 2nd and 3rd blood samples. GMTs were comparable between the subjects who seroconverted shortly after end of chemoprophylaxis compared to those subjects who became infected after chemoprophylaxis. 8 of 16 subjects who seroconverted during or shortly after chemoprophylaxis were asymptomatic during the entire period. Chemoprophylaxis appeared to have curtailed spread of nH1N1 within the affected units and did not appear to have increased the attack rate after end of chemoprophylaxis.

Major Compulsory Revisions

The timing of the blood collections is unclear. There were three outbreaks that started 1-2 weeks of each other. Perhaps in Table 2 information can be provided on the mean (SD) duration for each period. Also a seroconversion rate based on person-day should also be provided. This would be most helpful in comparing rates between the two time periods and would strengthen the discussion on the infection rate after post-exposure chemoprophylaxis. As currently described it is difficult to determine if there exists a beneficial or detrimental impact from the chemoprophylaxis strategy on the rate of infection post-chemoprophylaxis.

Minor Essential Revisions

It is unclear when subjects were allowed to return home for the weekend. Were
they allowed to visit their families during chemoprophylaxis or post-chemoprophylaxis? Please describe in text.

It is unclear if the subjects who seroconverted during the post-chemoprophylaxis period had symptomatic and/or asymptomatic infection. Please describe in text.

It would be helpful if the nomenclature to describe the periods during and after chemoprophylaxis were consistent throughout the manuscript. That used in Table 3 would be appropriate.

Were nH1N1 positive subjects who were sent home treated with oseltamivir? Did these individuals have serologic analysis performed even if they did not have an acute blood sample at baseline? If yes, it would be helpful to know their convalescent GMT. I would predict that they will have higher GMT compared to those subjects who developed breakthrough infection during chemoprophylaxis. This is because ill subjects who are treated are likely to have a higher total viral load compared to subjects who receive chemoprophylaxis and develop a breakthrough infection.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I receive grant support or have consulted for Roche, MedImmune, sanofi-pasteur, CSL, Novartis and Merck.