

*Neuraminidase Inhibitors: the Great Debate –
Panel Discussion*

Pandemics

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- 2009 pandemic was the first time that specific antivirals were available to treat illness or to slow the spread of pandemic influenza.
- In the USA during 2009, 8.7 million oseltamivir prescriptions (28.4 prescriptions /1000 persons) were dispensed from community pharmacies at a cost of US\$905 million (Suda et al.). Virtually all was from seasonal supply – not the pandemic stockpile.
- Although mortality during the pandemic was lower than initially anticipated, a unique opportunity was provided to review the effectiveness of oseltamivir in preventing widespread transmission of the pandemic virus and to determine the benefit of oseltamivir on patients who were hospitalized with confirmed A(H1N1)pdm09 virus infection.
- Such observational data were important because of the continued absence of placebo controlled RCT data on the effect of oseltamivir in severely ill or hospitalized patients.



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Suda et al. Pharmacotherapy 2015; 35(11):991-997



- Use of the NAIs in Japan is so widespread that almost every confirmed influenza case is treated, and is likely to have led to the extensive and rapid delivery in the 2009 pandemic.
- For example, in a study of Japanese children hospitalized with A(H1N1)pdm09 infections, more than 98% (984/1000) were treated with an NAI, and for those where the treatment time was recorded, 89% received NAIs within 48 hours and 70% within 24 hours. Only 1% of the hospitalized children ultimately required mechanical ventilation and one death was recorded (Suguya et al.).
- Pregnant Japanese women were treated prophylactically after close contact with an infected person and, if infected and hospitalized, over 90% were given NAIs within 48 hours of symptom onset. Compared to the high rates of mortality in pregnant women in many countries around the world (Burioni et al.), there were no maternal mortalities in Japan during the pandemic (Nakai et al.).
- Rapid access to stockpiled NAIs in a pandemic is important to achieve the greatest benefit from their use. In other countries, the pandemic of 2009 confirmed that centralized stockpiles did not facilitate rapid distribution (Gutierrez-Mendoza et al.)
- It is likely that decentralized stockpiles would be more efficient. Stockpiles in hospitals, would facilitate distribution, treatment of ill patients and allow periodic transfer of some material into 'seasonal' usage to avoid wastage



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Sugaya et al. J Infect 2011; 63(4):288-294

Burioni et al. Lancet 2009; 374(9699):1417-1418

Nakai et al. J Obstet Gynaecol Res 2012; 38(5):757-762.

Gutierrez-Mendoza et al. Bull WHO 2012; 90(10):782-787



Conclusions / discussion points

- Based on available evidence, oseltamivir should be used and stockpiled for the treatment of severe laboratory confirmed influenza in hospitalized patients. These stockpiles should be widely distributed to facilitate rapid use when needed.
- Only ecological evidence from Japan supports stockpiling of oseltamivir for widespread use in the community. Without a mechanism for rapid distribution of the drug in an emergency, any potential benefit of such large scale stockpiling will not be realized. Rapid distribution in an emergency is only likely if a mechanism exists for rapid distribution routinely.
- Observational study designs conducted for seasonal influenza should be readily adaptable to studies of pandemic influenza on very short notice. Prospective observational studies are more feasible than RCTs in an emergency response situation.
- In addition to data on outcome, such as risk of ICU admission and death, these observational studies should collect sequential data on markers of immune function in all recruited patients.



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