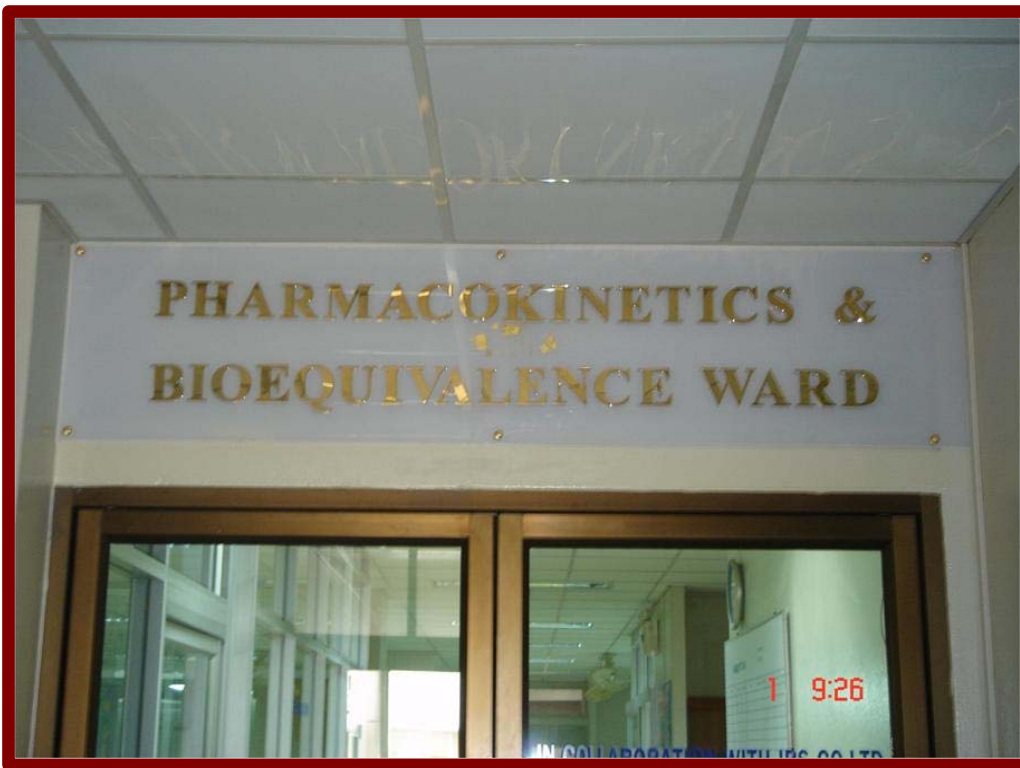


South East Asia Infectious Disease Clinical Research Network and Phase I studies









1. Pharmacologic study of Oseltamivir in Healthy Volunteer (completed 2007)
2. Open-Label Study to Evaluate Potential Pharmacokinetic Interactions Between Orally-Administered Oseltamivir and Intravenous Zanamivir in Healthy Thai Adult Subjects.



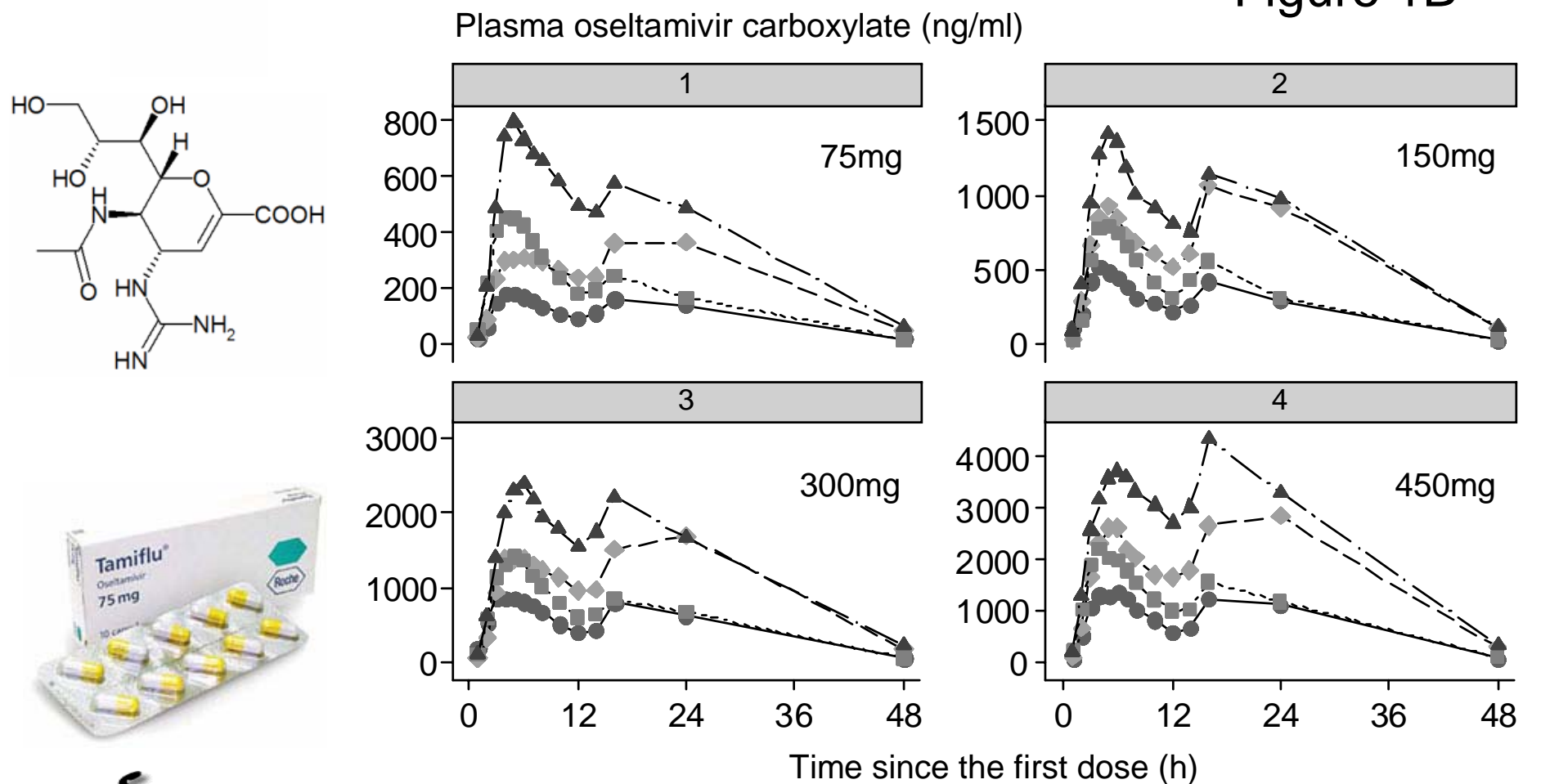


3. Open-Label Study to Evaluate Potential Pharmacokinetic of Oseltamivir in Healthy Thai Obese.
4. Open-Label Study to Evaluate Potential Pharmacokinetic of Intravenous Zanamivir in Healthy Thai Obese.

Pharmacokinetics of High-Dose Oseltamivir in Healthy Volunteers⁷

Y. Wattanagoon,¹ K. Stepniowska,^{1,2} N. Lindegårdh,^{2,1} S. Pukrittayakamee,¹ U. Silachamroon,¹

Figure 1B





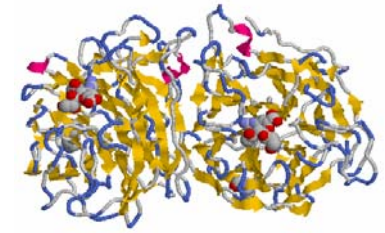
Main findings (1):

- oseltamivir phosphate (OP) is rapidly and reliably hydrolysed to the active carboxylate metabolite(OC).
- approximately 7 % of the dose is excreted in the urine before conversion.
- the OC metabolite is eliminated more slowly than the parent compound (OP).
- there was no evidence of dose-dependency in the kinetics over a nine-fold dose range from 75mg to 675mg.
- to attain therapeutic concentrations as rapidly as possible a loading dose should be given at least 25% higher than the maintenance dose

Main findings (2):



- effect of probenecid was consistent with a previous study reported by Hill et al 2002 - probenecid reduced urine clearance of OC more than 50%
- probenecid also contracted the total apparent volume of distribution by an average of 40 %
- these two independent effects resulted in a net 154 % increase in the OC AUC
- the effect of probenecid was consistent at all doses
- the contraction in the apparent volume of distribution caused by probenecid might suggest that transport to tissue compartments was reduced.
- saliva was sampled and did show relatively reduced concentrations in probenecid recipients.



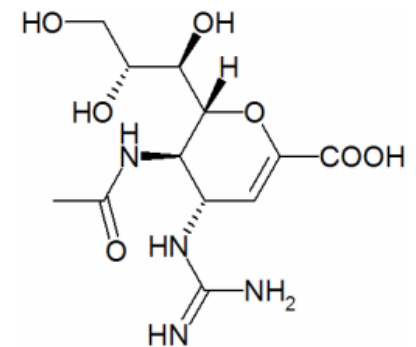
Zanamivir

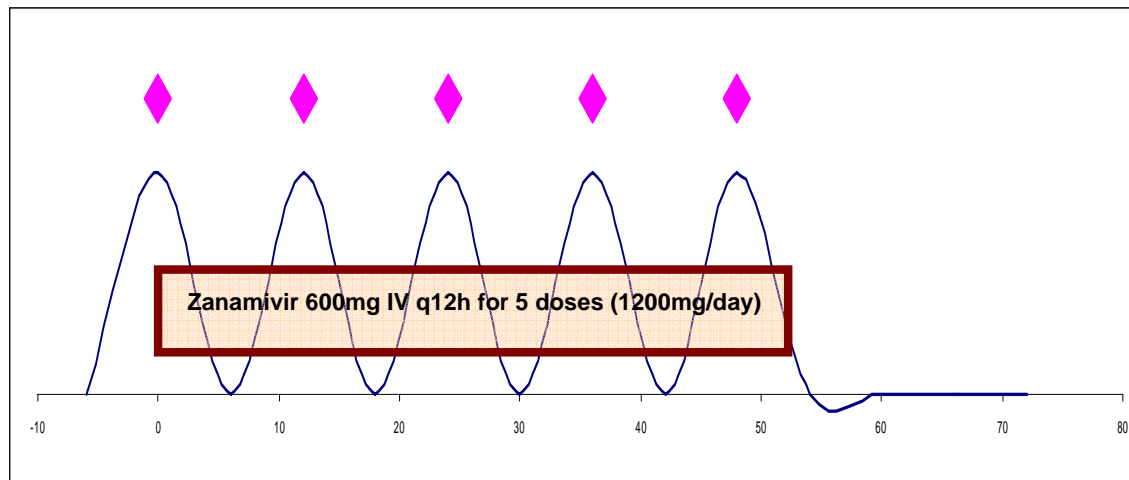
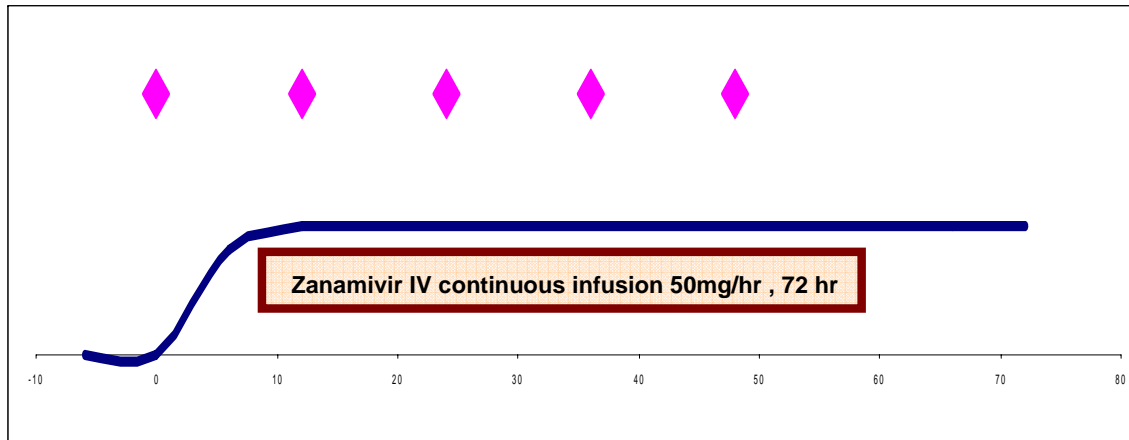
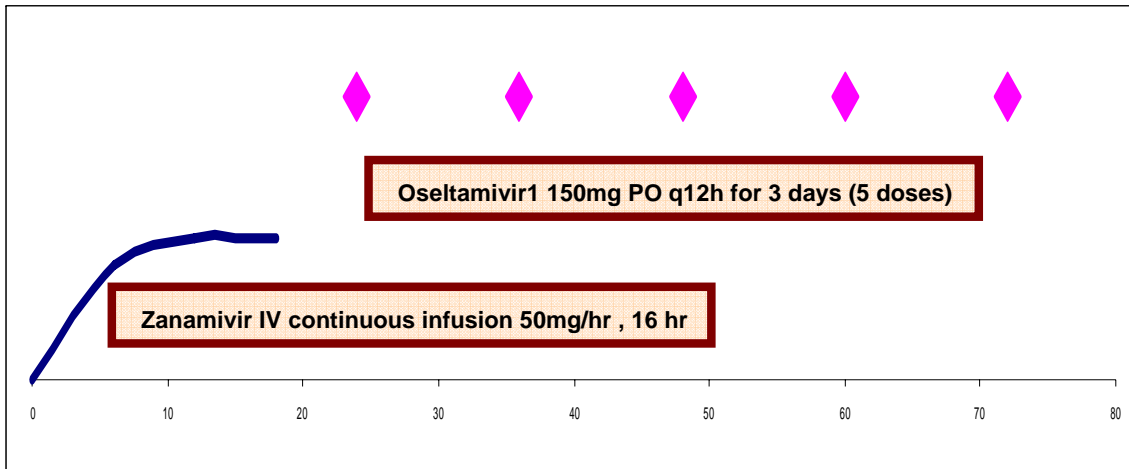
- A novel compound which inhibits the enzyme neuraminidase of both influenza A and B
- Very well tolerated by all routes of exposure
- The elimination half-life was about 1.7 hrs and 90% was excreted unchanged in the urine
- Six clinical pharmacology studies of IV zanamivir have been conducted, 1– 600 mg single dose and 600 mg twice daily for 5 days
- The most commonly reported adverse events were headache (14-38%), these were observed with similar frequency in placebo group



Open-Label Study to Evaluate Potential Pharmacokinetic Interactions Between Orally-Administered Oseltamivir and Intravenous Zanamivir in Healthy Thai Adult Subjects

- This study will provide clinical guidance for the use of intravenous Zanamivir in settings where oral Oseltamivir is commonly used





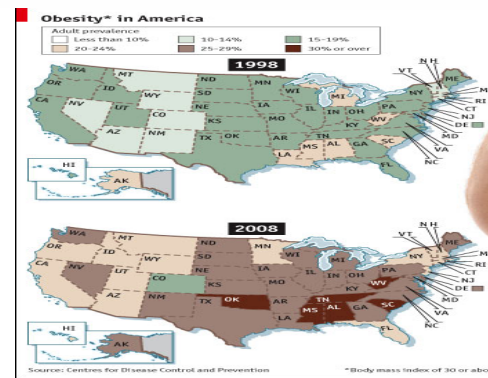


- *Intensive-Care Patients With Severe Novel Influenza A (H1N1) Virus Infection --- Michigan, June 2009.*
- *Hospitalized patients with novel influenza A (H1N1) viral infection---California, April-May 2009.*

Rapid communications

EPIDEMIOLOGY OF FATAL CASES ASSOCIATED WITH PANDEMIC H1N1 INFLUENZA 2009

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2. The members of the epidemic intelligence team at InVS are listed at the end of the article





3. Open-Label Study to Evaluate Potential Pharmacokinetic of Oseltamivir in Healthy Thai Obese.
4. Open-Label Study to Evaluate Potential Pharmacokinetic of Intravenous Zanamivir in Healthy Thai Obese.