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

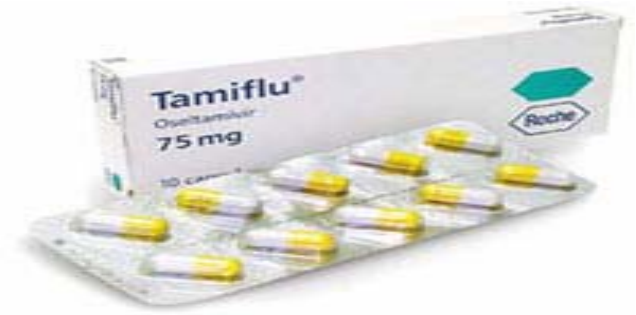

PHARMACOKINETICS &
BIOEQUIVALENCE WARD
1 9:26


SHARP


Thermo
1 9:19

SEA Influenza Clinical Research Network

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.



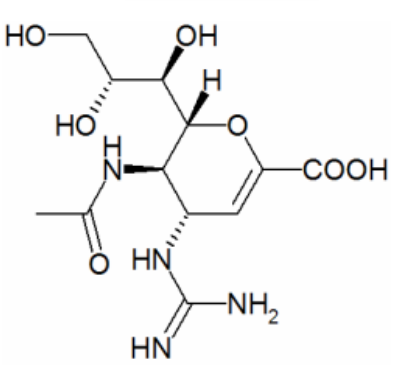
3. Open-Label Study to Evaluate Potential Pharmacokinetic of Oseltamivir in Healthy Thai Obese.
4. Open-Label Study to Evaluate Potential Pharmacokinetic of Intravenous Zanamivir in Healthy Thai Obese.

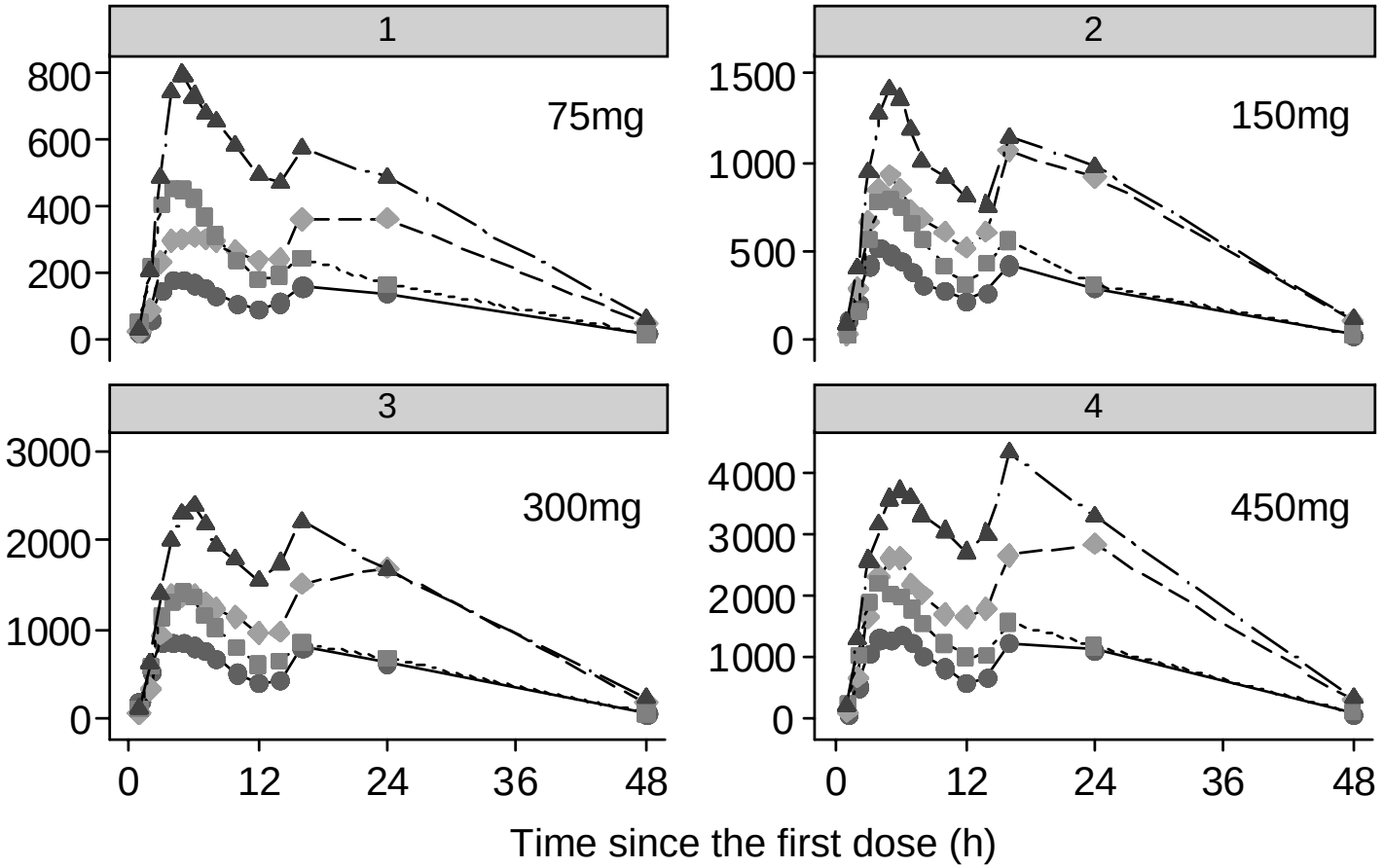
ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Mar. 2009, p. 945–952 Vol. 53, No. 3
0066-4804/09/$08.00+0 doi:10.1128/AAC.00588-08

Pharmacokinetics of High-Dose Oseltamivir in Healthy Volunteers[▽]

Y. Wattanagoon,[1] K. Stepniewska,[1,2] N. Lindegårdh,[2,1] S. Pukrittayakamee,[1] U. Silachamroon,[1]

Figure 1B





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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.

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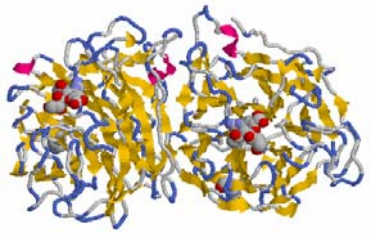
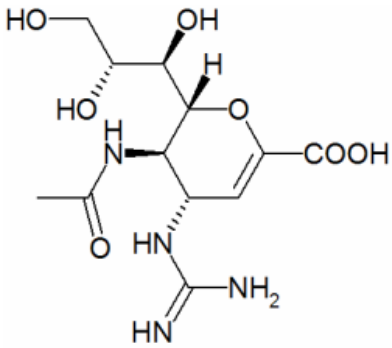


Zanamivir

- 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



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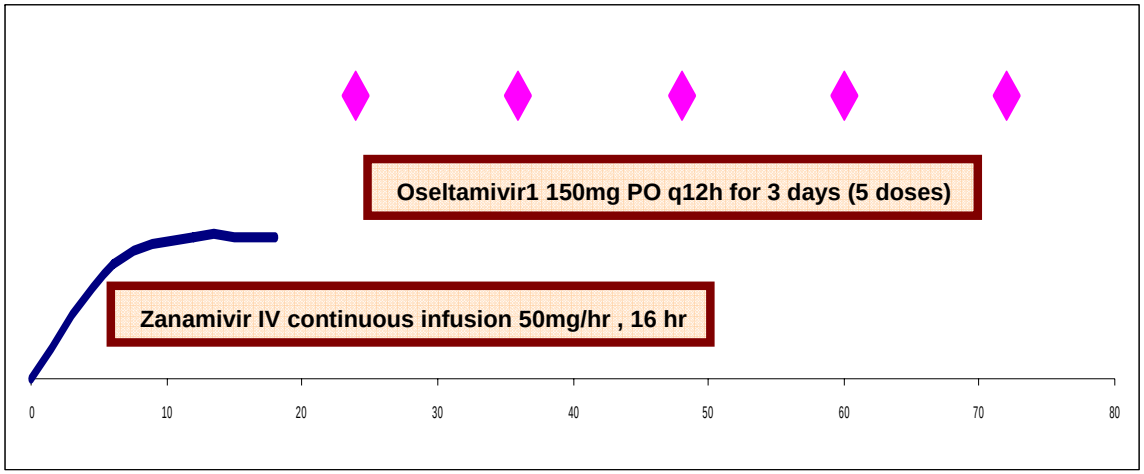
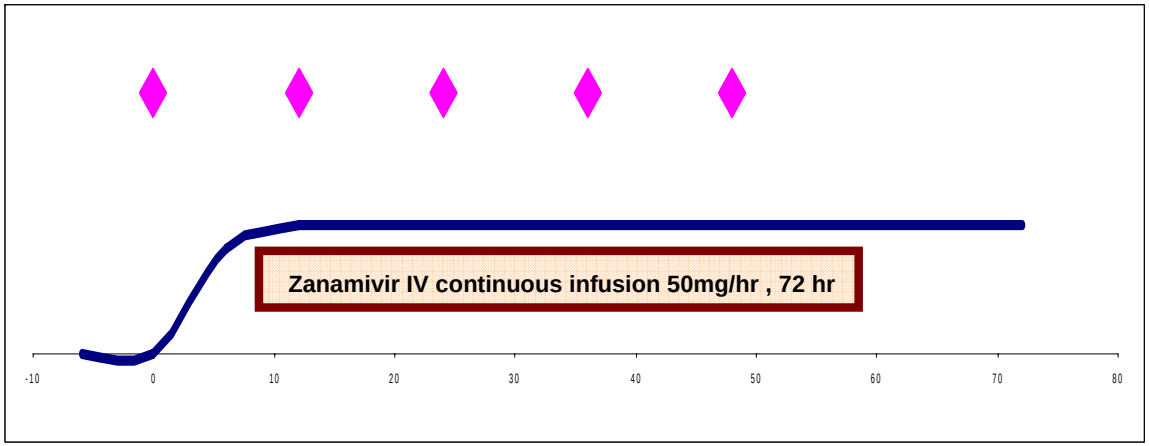
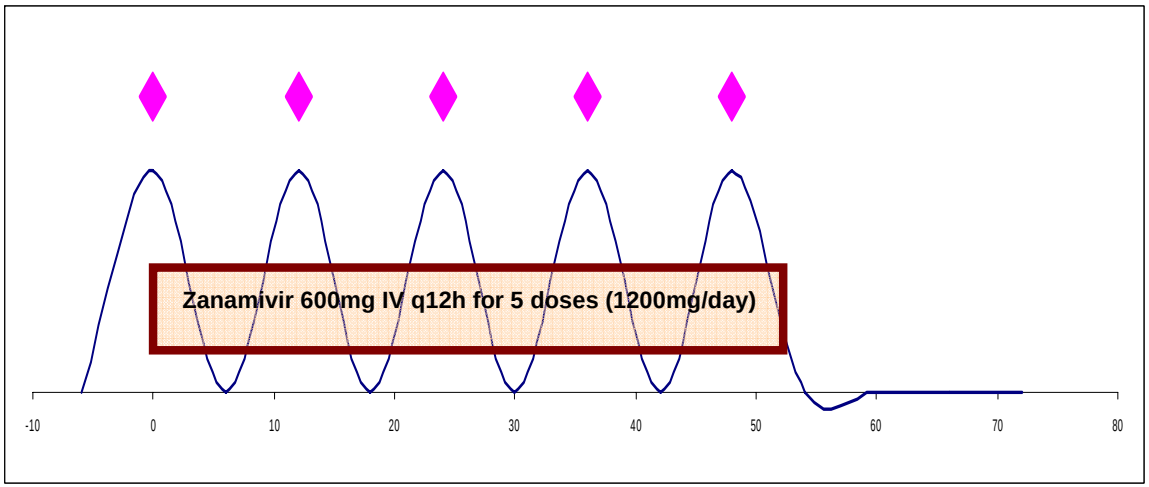

Oseltamivir1 150mg PO q12h for 3 days (5 doses)
Zanamivir IV continuous infusion 50mg/hr , 16 hr
0
10
20
30
40
50
60
70
80


Zanamivir IV continuous infusion 50mg/hr , 72 hr
-10
0
10
20
30
40
50
60
70
80


Zanamivir 600mg IV q12h for 5 doses (1200mg/day)
-10
0
10
20
30
40
50
60
70
80

- ***Intensive-Care Patients With Severe Novel Influenza A (H1N1) Virus Infection --- Michigan, June 2009.***
- ***Hospitallized 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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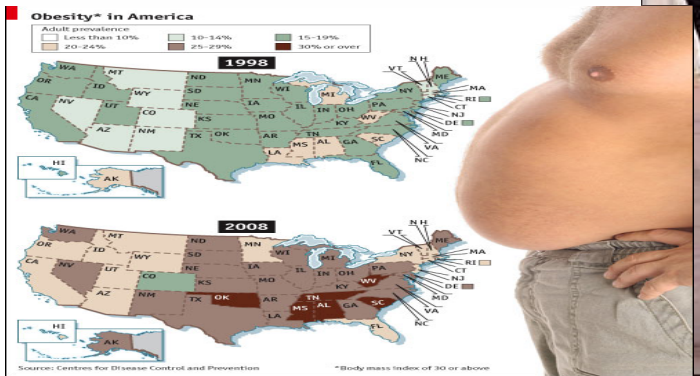
1. French Institute for Public Health Surveillance (Institut de Veille Sanitaire, InVS), St Maurice, France
2. The members of the epidemic intelligence team at InVS are listed at the end of the article



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