

EVMS Journal Club
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P: In patients presenting to the ED
I: Is the use of antivirals effective for treatment or prophylaxis of the flu
C: compared to symptomatic treatment alone
O: associated with improved time to resolution or complication rates

Search terms: seasonal, influenza, flu, treatment or prophylaxis, antiviral, oseltamivir , zanamivir

Scenario: On yet another busy shift you've seen another otherwise healthy person with flu-like symptoms, coughing, malaise, fevers requesting a prescription for

	Study	Patients	Outcomes	Positives	Negatives
Shun-Shin et al. Neuraminidase inhibitors for treatment and prophylaxis of influenza in children: systematic review and meta-analysis of randomized controlled trials 2009; 339 BMJ	Systemic review and meta analysis of randomized controlled trials	1766 children <12 with suspected flu 863 children post exposure prophylaxis	Time to resolution of illness incidence of flu in children living households with index cases of flu	4 treatment trials with reductions to sx resolution 0.5-1.5d, 3 trials post exposure treatment 8% reduction in incidence	Statistical significance noted only in 2 trials No change in abx use or asthma exacerbations
Cooper et al Effectiveness of neuraminidase inhibitors in tx and prevention of influenza A and B: systematic review and meta analysis of randomized controlled trials 2003 BMJ	Systematic review and meta analysis of randomized controlled trials 17 treatment 7 post-exp prophylaxis	Included: <12 years 12-65 healthy Chronic medical conditions or 65+	Median time to alleviation of sx Number of flu avoided	17 tx trials Reduction by group zanamivir 1d/0.8d/0.9d Oseltamivir 0.9/0.9/0.4 7 prevention trials demonstrated a 69% post exposure reduction	Primary efficacy was in otherwise healthy and not highly vulnerable Heterogeneity not reported Minimal shortening of sx 0.5-1.0 days

<p>Jefferson T et al</p> <p>Antivirals for influenza in healthy adults: systematic review</p> <p>2006 Volume 367, Issue 9507, Pages 303-313</p> <p><i>The Lancet</i></p>	<p>Systematic review and meta analysis of RCT</p> <p>four prophylaxis, 13 treatment and four post-exposure prophylaxis (PEP) trials</p>	<p>Randomized or quasi-randomized placebo-controlled studies of NIs in healthy adults exposed to naturally occurring influenza</p>	<p>Prophylaxis</p> <p>Efficacy against symptomatic flu</p> <p>Post exposure prophylaxis</p> <p>Median time to alleviation of sx</p>	<p>NIs have no effect against influenza-like (relative risk (RR) 1.28, 95% confidence interval (CI) 0.45 to 3.66 oseltamivir RR 1.51, 95% CI 0.77 to 2.95 zanamivir</p> <p>61% (RR 0.39, 95% CI 0.18 to 0.85) (tamiflu) Zanamivir 62%(RR 0.38, 95% CI 0.17 to 0.85).</p> <p>Oseltamivir 68% -89%. Zanamivir 62%</p> <p>1:33, zanamivir; 1:30 oseltamivir 48 h of sx onset</p>	<p>Oseltamivir at 150 mg daily was effective in preventing lower respiratory tract complications in influenza cases (OR 0.32, 0.18-0.57).</p>
<p>Kaiser et al</p> <p>Impact of Oseltamivir Treatment on Influenza-Related Lower Respiratory Tract Complications and Hospitalizations</p> <p>2003;163:1667-1672.<i>Arch Intern Med.</i></p>	<p>Prospective controlled data in 10 placebo controlled double blind trials of oseltamivir tx</p>	<p>People age range, 13-97 years with influenza-like illness</p>	<p>LRTCs and antibiotic use</p> <p>High risk pt and abx use</p>	<p>reduced overall abx use for any reason 26.7% (14.0% vs 19.1%) LRTC abx by 55% (4.6% vs 10.3%)</p> <p>High risk pt 74 (18.5%) of 401LRTC leading abx compared with 45 (12.2%) of 368 oseltamivir $P = .02$)</p>	<p>No change in unconfirmed cases of flu</p>
<p>Orzeck EA al</p> <p>Oseltamivir and the risk of influenza-related complications and hospitalizations in patients with diabetes</p> <p>2007; 29:2246-55. <i>Clin Ther</i></p>	<p>subgroup analysis of a retrospective cohort study</p>	<p>9090 patients with diabetes and a diagnosis of influenza</p>	<p>2919 (32%) received a prescription for oseltamivir and 6171 (68%) received no antiviral treatment.</p>	<p>17% reduction in the risk of respiratory illnesses (RR = 0.83; 95% CI, 0.73-0.93) 30% reduction in the risk of hospitalization for any reason (RR = 0.70; 95% CI, 0.52-</p>	<p>No change in pna, OM, of pneumonia hospitalizations</p>

<p>Lalezari et al</p> <p>Zanamivir for the Treatment of Influenza A and B Infection in High-Risk Patients 2001;161:212-217. <i>Arch Intern Med.</i></p>	<p>retrospective</p>	<p>high-risk patients in studies 1998–1999 winter season</p>	<p>Return to normal activities</p> <p>Symptom severity</p> <p>antibiotic use</p>	<p>2.5 days compared with those given placebo 3.0 days earlier ($P = .022$)</p> <p>11% reduction ($P = .039$)</p> <p>Dec by 43% ($P = .045$)</p>	<p>severity and return to activity data minimal</p> <p>Abx use decreased</p>
<p>Blumentals et al</p> <p>Impact of oseltamivir on the incidence of secondary complications of influenza in adolescent and adult patients: results from a retrospective population-based study</p>	<p>Retrospective cohort analysis utilizing health insurance claims data in the USA</p>	<p>36 751 eligible patients</p>	<p>influenza-related secondary complications in otherwise healthy</p>	<p>OM by 23% (HR=0.77; 95% CI: 0.65, 0.93),</p> <p>respiratory disease by 18% (HR 0.82; 95% CI: 0.79, 0.86),</p> <p>hospitalization 22% (HR 0.78; 95% CI: 0.67, 0.91).</p>	<p>no differences in any other clinical outcomes, including hospitalization for respiratory disease.</p>

Clinical Bottom Line: Antivirals appear to offer small advantages in decreasing duration of illness and appear to offer no advantage to otherwise healthy subjects. These agents may be more efficacious in those requiring post-exposure prophylaxis
-In view of limited impact on disease duration as well as recently noted resistance patterns to seasonal influenza, avoiding treatment of low risk populations is probably warranted.

Current CDC Recommendations as of 10/1/09 for flu treatment or chemoprophylaxis

Treatment with oseltamivir or zanamivir for all persons with suspected or confirmed influenza requiring hospitalization.
Early empiric treatment with oseltamivir or zanamivir who are at higher risk for complications including:
Children younger than 2 years old;
Persons aged 65 years or older
Pregnant women
Persons of any age with certain chronic medical or immunosuppressive conditions; and,
Persons younger than 19 years of age who are receiving long-term aspirin therapy.