# Oseltamivir was safe and effective for prophylaxis of influenza in the frail elderly

Peters PH Jr, Gravenstein S, Norword P, et al. **Long-term use of oseltamivir for the prophylaxis of influenza in a vaccinated frail older population.** J Am Geriatr Soc. 2001 Aug;49:1025-31.

### QUESTION

In frail older persons in a residential setting, is oseltamivir (a neuraminidase inhibitor) safe and effective in preventing influenza A and B?

### DESIGN

Randomized (allocation concealed*), blinded (clinicians and participants),* placebo-controlled trial with 8-week follow-up.

### SETTING

31 residential homes or sheltered accommodations for seniors in 5 countries during the 1998–99 influenza season.

### PARTICIPANTS

572 persons who were ≥ 65 years of age, resided in care homes for seniors, and scored ≥ 7 on a Mental Status Questionnaire. Exclusion criteria included antibiotic therapy for acute upper respiratory tract infection, otitis media, bronchitis, or sinusitis and antiviral therapy for influenza in the previous 2 weeks. 548 persons (mean age 81 y, 69% women), of whom 80% were vaccinated against influenza, received ≥ 1 dose of study drug and were included in the intention-to-treat analysis.

### INTERVENTION

Participants were stratified by influenza vaccination status and coexisting chronic obstructive airway disease and allocated to oseltamivir, 75 mg once daily for 6 weeks ($n$ = 276), or placebo ($n$ = 272) when local influenza activity was detected.

### MAIN OUTCOME MEASURES

Laboratory-confirmed clinical influenza (temperature ≥ 37.2°C plus 1 respiratory symptom [cough, sore throat, or nasal congestion] and 1 constitutional symptom [aches and pains, fatigue, headache, or chills or sweats]). Secondary outcomes were symptomatic laboratory-confirmed influenza not meeting the criteria for clinical influenza, asymptomatic laboratory-confirmed influenza infection, influenza-like illness, and complications of influenza.

### MAIN RESULTS

Fewer patients who received oseltamivir had laboratory-confirmed clinical influenza than did those who received placebo ($P$ = 0.002) (Table). The groups did not differ for laboratory-confirmed influenza, including all clinical cases; influenza not meeting clinical criteria; and asymptomatic influenza ($P$ = 0.18) or acute respiratory illness other than influenza {$P$ = 0.75}†. Fewer oseltamivir-group patients had complications of influenza than did placebo-group patients ($P$ = 0.037) (Table). The groups did not differ for adverse events (84% vs 89%), 90% of which were of mild-to-moderate intensity.

### CONCLUSION

In frail older persons, oseltamivir was safe and effective in preventing influenza A and B.

*Source of funding: F. Hoffmann-La Roche AG.*

*For correspondence: Dr. P.H. Peters, Jr., South Texas Medical Research Associates, 6547 Bandera Road, Suite C, San Antonio, TX 78238, USA.* ■

*See Glossary.

†*P* value calculated from data in article.

**Oseltamivir vs placebo for influenza prophylaxis in frail older persons‡**

| Outcomes at 8 wk | Oseltamivir | Placebo | RRR (95% CI) | NNT (CI) |
|---|---|---|---|---|
| Laboratory-confirmed clinical influenza | 0.4% | 4.4% | 92% (51 to 99) | 25 (14 to 56) |
| Influenza complications | 0.4% | 2.6% | 86% (13 to 98) | 45 (21 to 380) |

‡Abbreviations defined in Glossary; NNT and CI calculated from data in article.

## COMMENTARY

Residents of long-term care facilities for the elderly are at high risk for influenza-related complications (1). In addition, because influenza vaccine is of limited efficacy in frail older persons (2), nursing-home influenza outbreaks remain common despite routine vaccination of residents. We therefore need to know whether additional benefit exists for antiviral prophylaxis in this setting.

The study by Peters and colleagues shows that oseltamivir is effective in preventing febrile illness caused by influenza and influenza complications in the elderly. Reducing complications is important because the complications of influenza rather than the disease itself are the cause of death and hospitalization. In contrast to studies in younger populations (3), no excess of nausea and vomiting occurred in the oseltamivir group in this study. Oseltamivir thus joins the list of medications that are effective in preventing influenza and its complications in residents of long-term care facilities; the others are the M2 inhibitors amantadine and rimantadine as well as zanamivir, another neuraminidase inhibitor.

Both Canadian and U.S. guidelines recommend the use of antiviral prophylaxis during influenza outbreaks (4, 5). Neuraminidase inhibitors are clearly indicated in situations in which M2 inhibitors are ineffective (outbreaks caused by influenza B and those caused by influenza A resistant to M2 inhibitors) or for patients in whom M2 inhibitors are contraindicated. For routine prophylaxis against influenza A, the appropriate choice of antiviral agent is not as clear. Neuraminidase inhibitors are associated with fewer side effects and less selection for resistance than are M2 inhibitors. However, whether these differences are substantial enough to warrant the additional cost of a neuraminidase inhibitor is unknown.

*Allison McGeer, MD, MSc*
*Mount Sinai Hospital*
*Toronto, Ontario, Canada*

***References***

1. **Cox N, Subbarao K.** Influenza. Lancet. 1999;354:1277-82.
2. **Gross PA, Hermogenes QW, Sacks HS, Lau J, Levandowski RA.** The efficacy of influenza vaccine in elderly persons. A meta-analysis and review of the literature. Ann Intern Med. 1995;123:518-27.
3. **Hayden FG, Atmar RL, Schilling M, et al.** Use of the selective oral neuraminidase inhibitor oseltamivir to prevent influenza. N Engl J Med. 1999; 341:1336-43.
4. **Centers for Disease Control and Prevention.** Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep. 2000;49:1-38.
5. **National Advisory Committee on Immunization (NACI), Health Canada.** Statement on influenza vaccination for the 2000-2001 season. Can Commun Dis Rep. 2000;26:1-16.