Zanamivir + Oseltamivir in moderate to severe ILI

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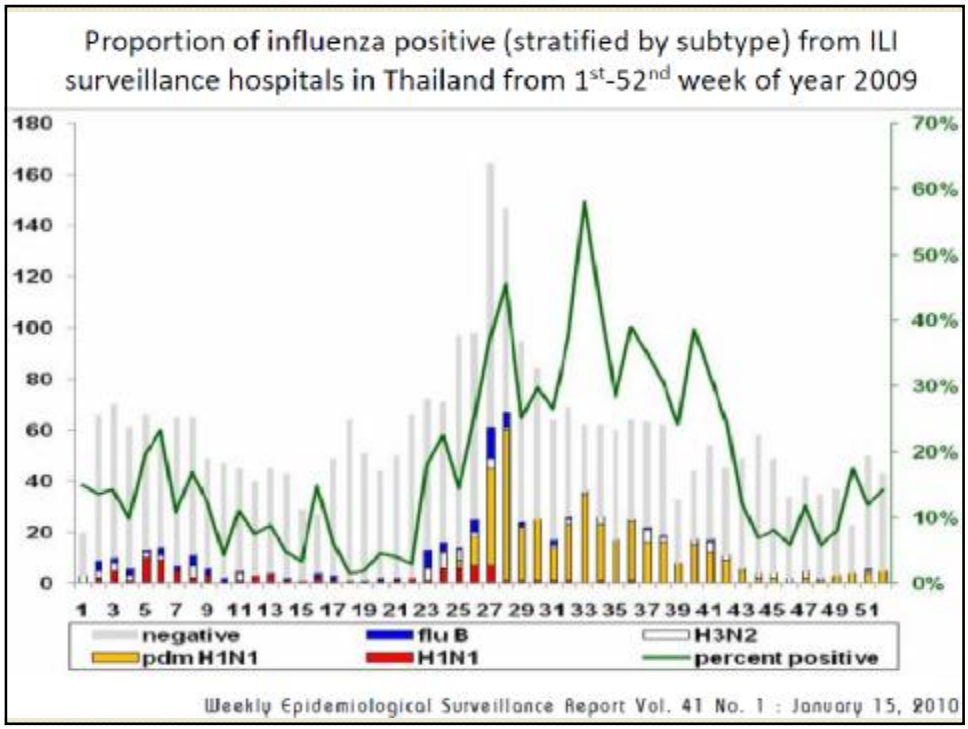
สถาบันสุขภาพเด็กแห่งชาติมหาราชินี

Zanamivir + Oseltamivir

- **What is/are the benefit?**
  - ILI due to influenza
  - Oseltamivir resistance influenza
- **What is/are the risk (complications)?**



Proportion of influenza in IPD

Authors	Years	Inclusions	Age	Lab	% influenza
Sunakorn P, et al	1988-89	226 LRTI	< 5 y	IFA	**0.4**
Suwanjutha S, et al	1989-90	596 LRTI	< 5 y	IFA	**4.2**
Chantarojanasiri T, et al	1992-93	210 pneumonia	< 5 y	IFA	**7.1**
Siritantikorn, et al	1998-01	472	< 5 y	IFA	**1**
Simmerman M, et al	2003-04	761 pneumonia	All age	PCR, Culture serology	**12**
Suntarattiwong P, et al	2004-05	456 LRTI & ILI	< 5 y	Culture	**8.6**
Samransamruajkit R, et al	2006-07	134 pneumonia	1-15 y	PCR	**12**
Chotpitayasunondh T, et al	2007-09	354 LRTI	< 1 y	PCR	**7.3**

Antiviral recommendation

- **Oseltamivir should be given in;**

1.

- มีอาการรุนแรง
- ปอดบวม
- ซึม ขาดน้ำ
- อาการไม่ดีขึ้นเลย หลัง 48 ชั่วโมง

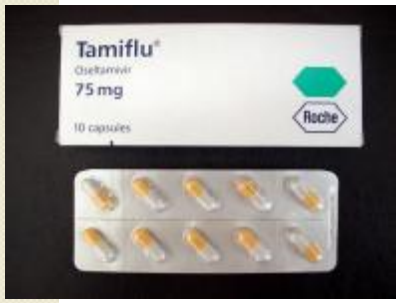
2.

- กลุ่มที่เสี่ยงมาก
  - หญิงตั้งครรภ์ โรคอ้วน
  - มีโรคเรื้อรัง: หอบหืด ระบบหัวใจและหลอดเลือด

Antiviral recommendation

3.

- กลุ่มที่เสี่ยงน้อย
  - อายุ **< 2** ปี หรือ **> 65** ปี
  - เบาหวาน ความดันที่ควบคุมได้
  - ติดเชื้อเอช ไอ วีที่ **CD4** ปกติ
  - โรคระบบประสาทที่ผู้ป่วยดูแลตัวเองได้ ไม่มีปัญหาด้านการสำลัก
- อาจพิจารณาให้ยาทันที หรือเฝ้าระวังอาการ ให้ถ้าไม่ดีขึ้นใน **48** ชม.



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Oseltamivir resistance influenza

Antiviral Resistance Testing Results on Samples Collected Since September 1, 2009.

	Viruses tested (n)	Resistant Viruses, Number (%) Oseltamivir	Viruses tested (n)	Resistant Viruses, Number (%) Zanamivir	Isolates tested (n)	Resistant Viruses, Number (%) Adamantanes
Seasonal Influenza A (H1N1)	1	1 (100.0)	0	0 (0)	1	0 (0)
Influenza A (H3N2)	8	0 (0)	0	0 (0)	11	9 (81.8)
Influenza B	1	0 (0)	0	0 (0)	N/A*	N/A*
2009 Influenza A (H1N1)	2,926	39[T1] (1.3)	830	0 (0)	837	834 (99.6)

http://www.cdc.gov/flu/weekly/

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

5 FEBRUARY 2010, 85th YEAR / 5 FÉVRIER 2010, 85e ANNÉE
No. 6, 2010, 85, 37–48
http://www.who.int/wer

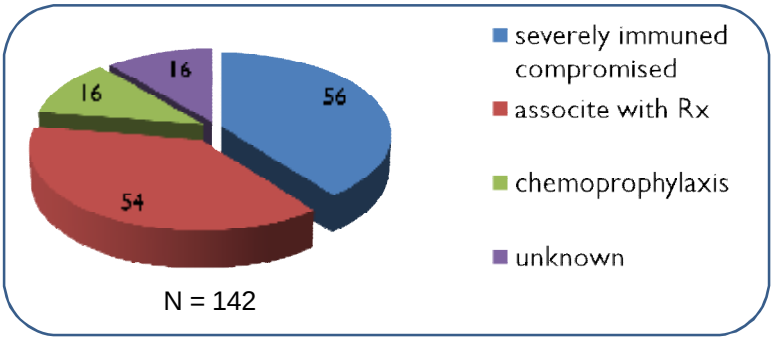
Table 1 **Geographical distribution of oseltamivir-resistant pandemic (H1N1) 2009 viruses, February 2010**
Tableau 1 **Répartition des virus de la grippe pandémique A(H1N1) 2009 résistants à l'oseltamivir (février 2010)**

Isolates – Isolements	WHO region – Région de l'OMS					
	Americas – Amériques	European – Europe	Eastern Mediterranean – Méditerranée orientale	African – Afrique	South-East Asia – Asie du Sud-Est	Western Pacific – Pacifique occidental
No. of isolates tested for antiviral susceptibility* – Nombre d'isolements pour lesquels on a testé la sensibilité*	>8000	>7500	50	66	20	>7500
No. of oseltamivir-resistant isolates reported – Nombre d'isolements résistants à l'oseltamivir qui ont été notifiés	65	77	1	0	0	82

* Data compiled from information provided by WHO Collaborating Centres for Reference and Research on Influenza, National Influenza Centres and from published reports from national health agencies. – Données compilées à partir des informations fournies par les Centres collaborateurs de l'OMS de référence et de recherche pour la grippe, les Centres nationaux de la grippe et à partir des rapports publiés par les organismes nationaux de santé publique.

Oseltamivir resistance influenza

- 225 cases reported worldwide
- H275Y mutation



http://www.who.int/wer

Oseltamivir resistance influenza

- ไข้หวัดใหญ่ตามฤดูกาล A/H1N1
- H274Y mutation
- Transmissible
- มีความสัมพันธ์กับผลการรักษาในทางคลินิกหรือไม่ ???

J Infect Dis 2006; 193: 760-4.
JAMA 2009; 301: 1034-41.
N Eng J Med 2009; 361: 2296-7.
Weelkly epidemiological record 2010; 85: 37-40

Zanamivir + Oseltamivir

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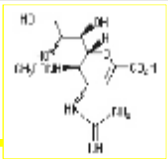
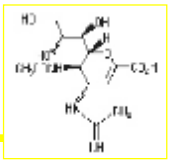
Zanamivir



- Zanamivir is a white to off-white powder for oral inhalation
- Each blister containing a powder mixture of 5 mg of zanamivir and 20 mg of lactose (which contains milk proteins)

Zanamivir (Relenza®) package insert

Zanamivir



- The amount of drug delivered to the respiratory tract will depend on patient factors such as inspiratory flow
- ROTADISK delivers 4 mg of zanamivir from the DISKHALER device when tested at a pressure drop of 3 kPa (corresponding to a flow rate of about 62 to 65 L/min) for 3 seconds

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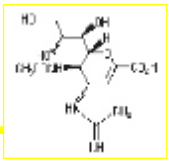
Zanamivir



- 8 of the 16 children (including all those under 8 years old) either did not produce measurable inspiratory flow through the DISKHALER
- Or produced peak inspiratory flow rates below the 60 L/min considered optimal for the device

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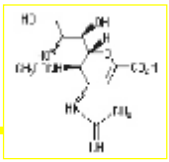
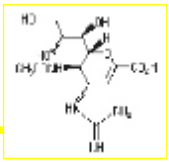
Zanamivir



- Reported side effects
  - Nasal signs and symptoms
  - Cough
  - Throat/tonsil discomfort and pain
  - were reported more frequently with RELENZA than placebo
  - Serious cases of bronchospasm, including fatalities, have been reported during treatment with RELENZA in patients with and without underlying airways disease

Zanamivir (Relenza®) package insert

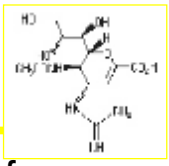
Zanamivir



- Reported side effects
  - Allergic-like reactions
  - Including oropharyngeal edema
  - Serious skin rashes
  - And anaphylaxis
  - Reported in postmarketing experience with RELENZA

Zanamivir (Relenza®) package insert

Zanamivir



- RELENZA is not recommended for treatment of influenza in individuals with underlying airways disease (such as asthma or COPD) due to risk of serious bronchospasm

- RELENZA has not been proven effective for treatment of influenza in individuals with underlying airways disease

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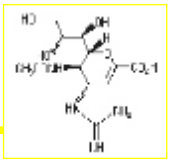
Zanamivir



- No information is available regarding treatment of influenza in;

- Patients with any medical condition sufficiently severe or unstable to be considered at imminent risk of requiring inpatient management

Zanamivir (Relenza®) package insert

Oseltamivir

zanamivir

World Health Organization

Clinical management of human infection with pandemic (H1N1) 2009: revised guidance

November 2009

In patients who have persistent severe illness despite oseltamivir treatment, there are few licensed alternative antiviral treatments. In these situations, clinicians have considered intravenous administration of alternative antiviral drugs such as zanamivir, peramivir, ribavirin, or other experimental treatments. The use of such treatments are used should be done only in the context of prospective clinical and virological data collection and with regard to the following cautions:

- ribavirin should not be administered as monotherapy;
- ribavirin should not be administered to pregnant women; and
- zanamivir formulated as a powder for inhalation should not be delivered via nebulization due to the presence of lactose, which may compromise ventilator function.