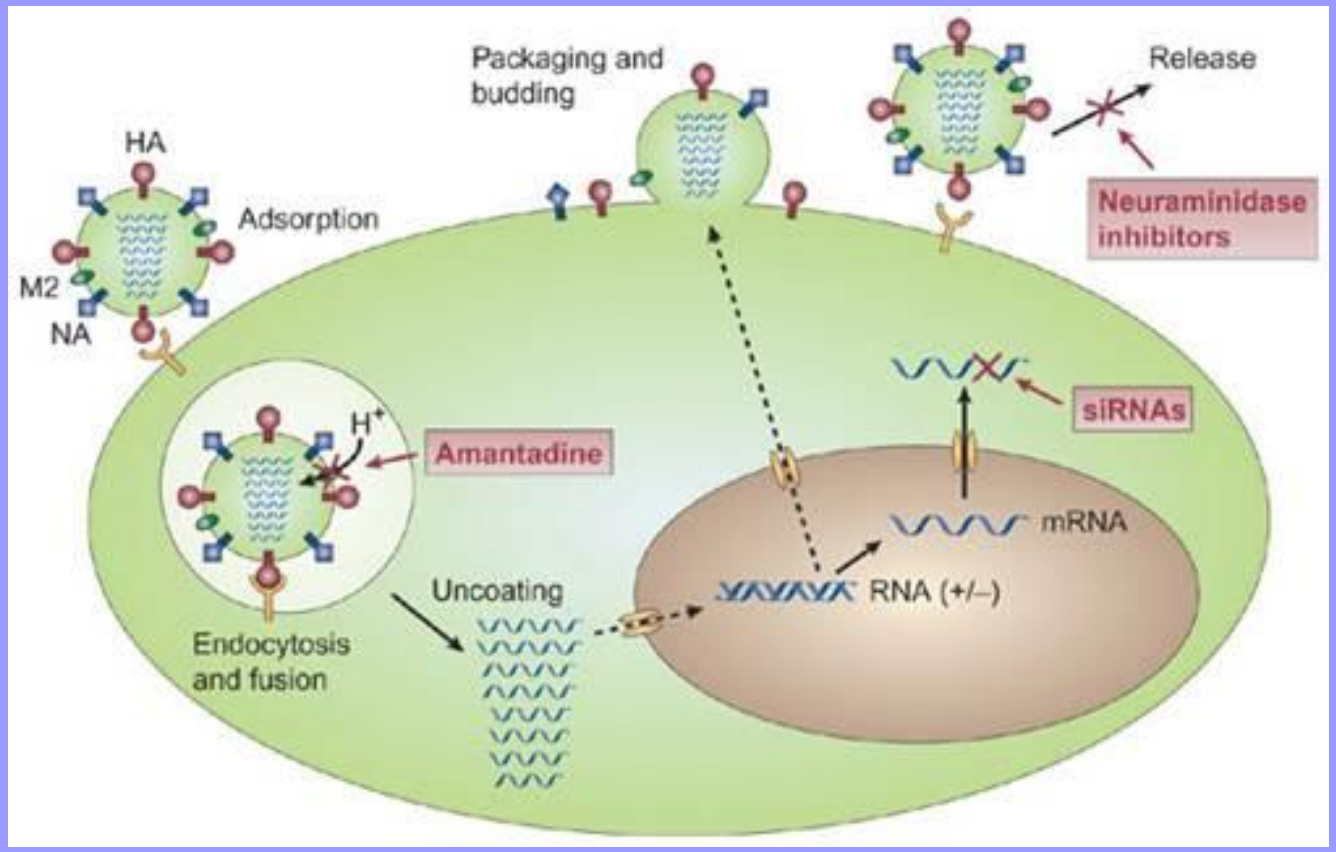
12/08/09

ZANAMIVIR

ITAI GUETA

ZANAMIVIR
Mechanism of Action

Neuroaminidase Inhibition



ZANAMIVIR
USES

-Influenza A or B

-For the symptomatic treatment of uncomplicated acute illness

-Adults, adolescents and children > 7 y/o (~5-8 y/o)

-Symptomatic for < 2 days

-For the prophylaxis of Influenza A/B virus Infections >5 y/o

ZANAMIVIR
EFFICACY

Treatment Efficacy*

Adults >12 y/o – decreased by 1.5 days

High risk patients** – decreased by 3 days

Children – decreased by 1.25 days

Prophylaxis Efficacy

Adults - 6% (34/554) placebo vs 2% (11/553) Zanamivir

Was not been shown to prevent bacterial complications

ZANAMIVIR ADMINISTRATION

-Inhalation

-As Treatment: 10 mg bid (= twice daily 2 consecutive inhalations of on 5mg blister) for 5 days.

-On 1st day of treatment – 2 doses in 2 hours apart

-Following days – 12 hours apart.

-As prophylaxis – once per day.

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ZANAMIVIR PHARMACOKINETICS

- Peak Pconc. 1-2 hours
- Extremely low Oral bioavailability.
- 10-20% active compound reaches the lungs.
- 4-7% of inhaled dose is systemically absorbed.
- <10% plasma protein binding
- $T_{½}$: 2.5 – 5/1 hours.

ZANAMIVIR
ADVERSE EFFECTS

BRONCHOSPASM

- Not for individuals with underlying airway disease (COPD, Asthma)

  Severe bronchospasm including fatalities in postmarketing.

  Phase I – 1/13 with mild to moderate asthma

  Phase III – 10% Zanamivir, 9% Placebo → 20% ↓ FEV1

ALLERGIC REACTIONS

- oropharyngeal edema, skin rashes, urticaria, anaphylaxis

  (Postmarketing)

NEUROPSYCHIATRIC EVENTS

- delirium and abnormal behvaior leading to injury (Japan, pediatrics)

	ZANAMIVIR inh	PLACEBO
Headaches	2%	2%
Diarrhea	3%	4%
Nausea	3%	3%
Vomiting	1%	2%
Nasal signs	2%	3%
Cough	2%	3%
Bronchitis	2%	3%
URT infections	2%	2%
Dizziness	2%	<1%

Most Frequent – ELE, CPK, Lymphopenia, Neutopenia (=)

ZANAMIVIR
DRUG INTERACTIONS

1. Not metabolized by CYP

2. Low serum concentrations and modest systemic exposure
3. Secreted unchanged by kidneys, yet in CRF – accumulation ?

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