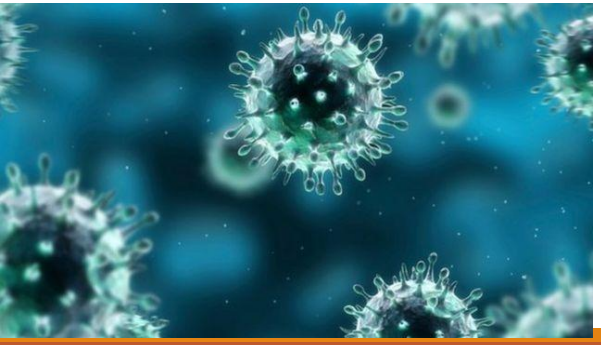
流感藥物治療進展與抗藥

成大醫院內科部感染科主治醫師

冉浩恩 2026.09.03

HAOEN JAN
Division of Infectious Diseases
National Cheng Kung University Hospital
Sep. 03, 2026

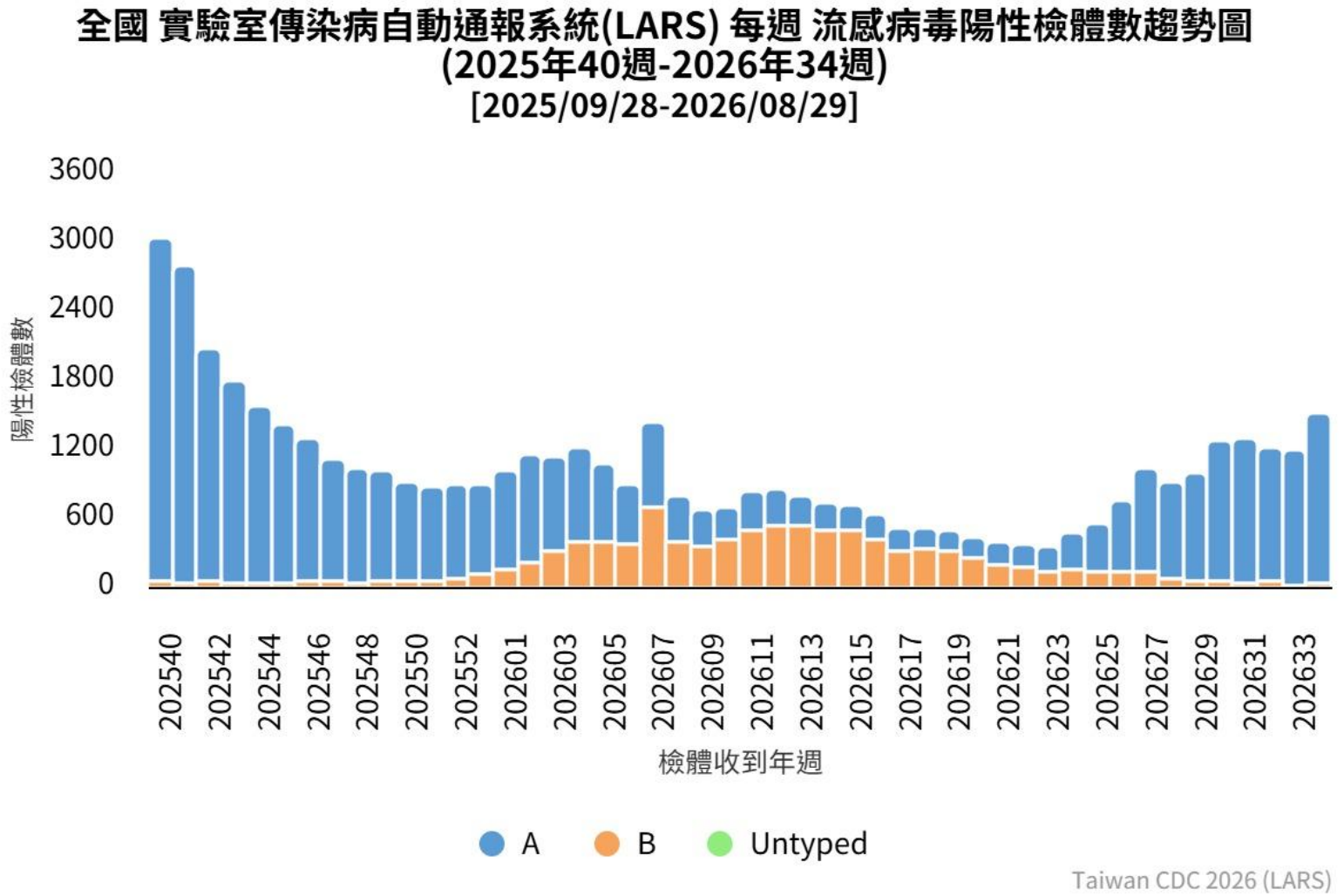


Outline

- 抗流感病毒藥物機轉及實證
- 流感藥物治療建議及實證更新
- 抗流感病毒藥物抗藥性現況

台灣現在：2026 夏末流感再度上升

LARS 到 2026/8/29；社區目前以 A(H1N1) 為主



2026 第34週

101,628

類流感門急診就診人次

+5.6% 較前週；近期緩升

A(H1N1) 74.1%

目前社區流行型別

8/25–8/31

新增重症 85 例

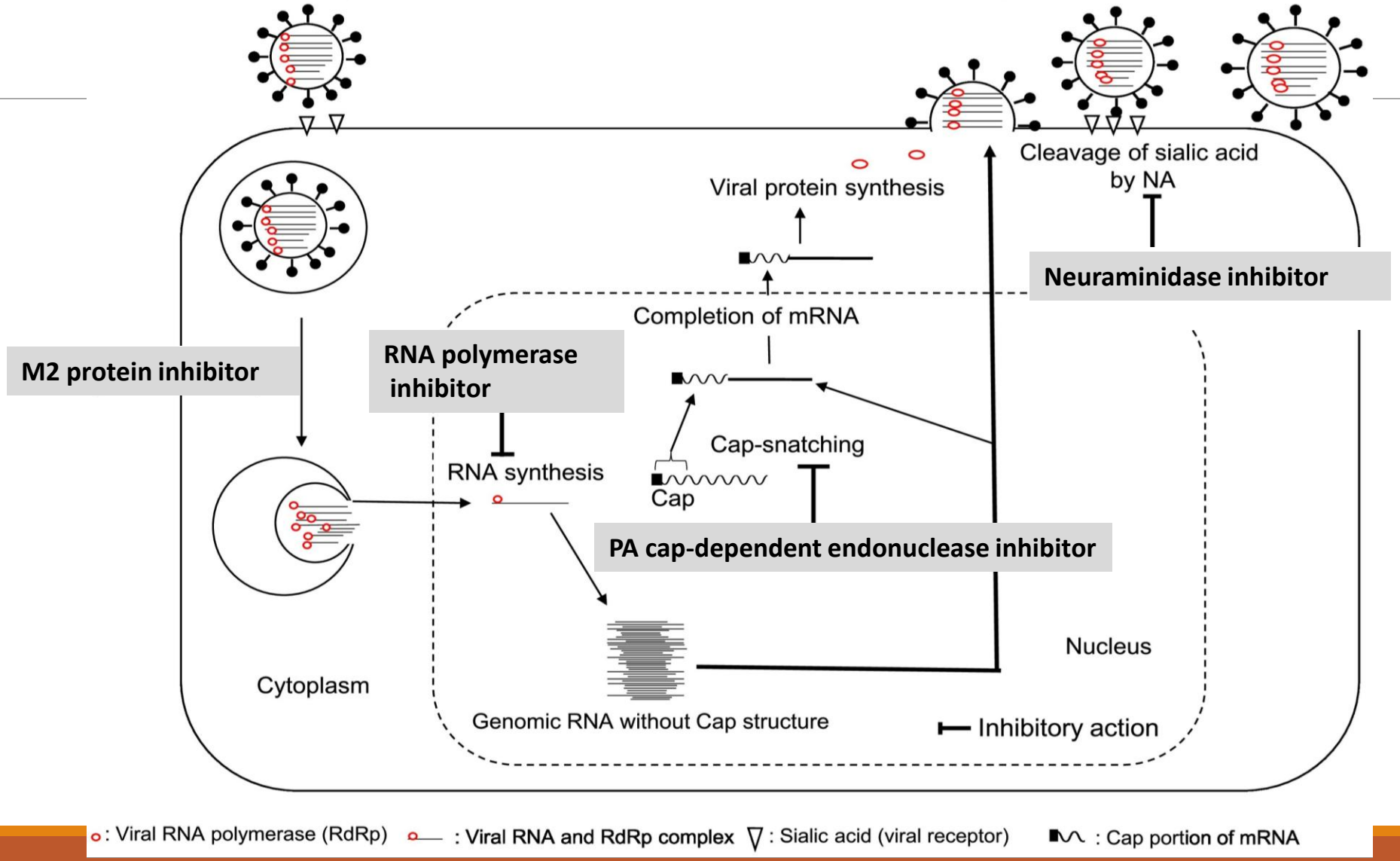
其中 80 例 H1N1

新增死亡 14 例

重症：65歲以上長者(占64.6%)及具慢性病史者(占82.8%)，69.4%未接種本季流感疫苗。

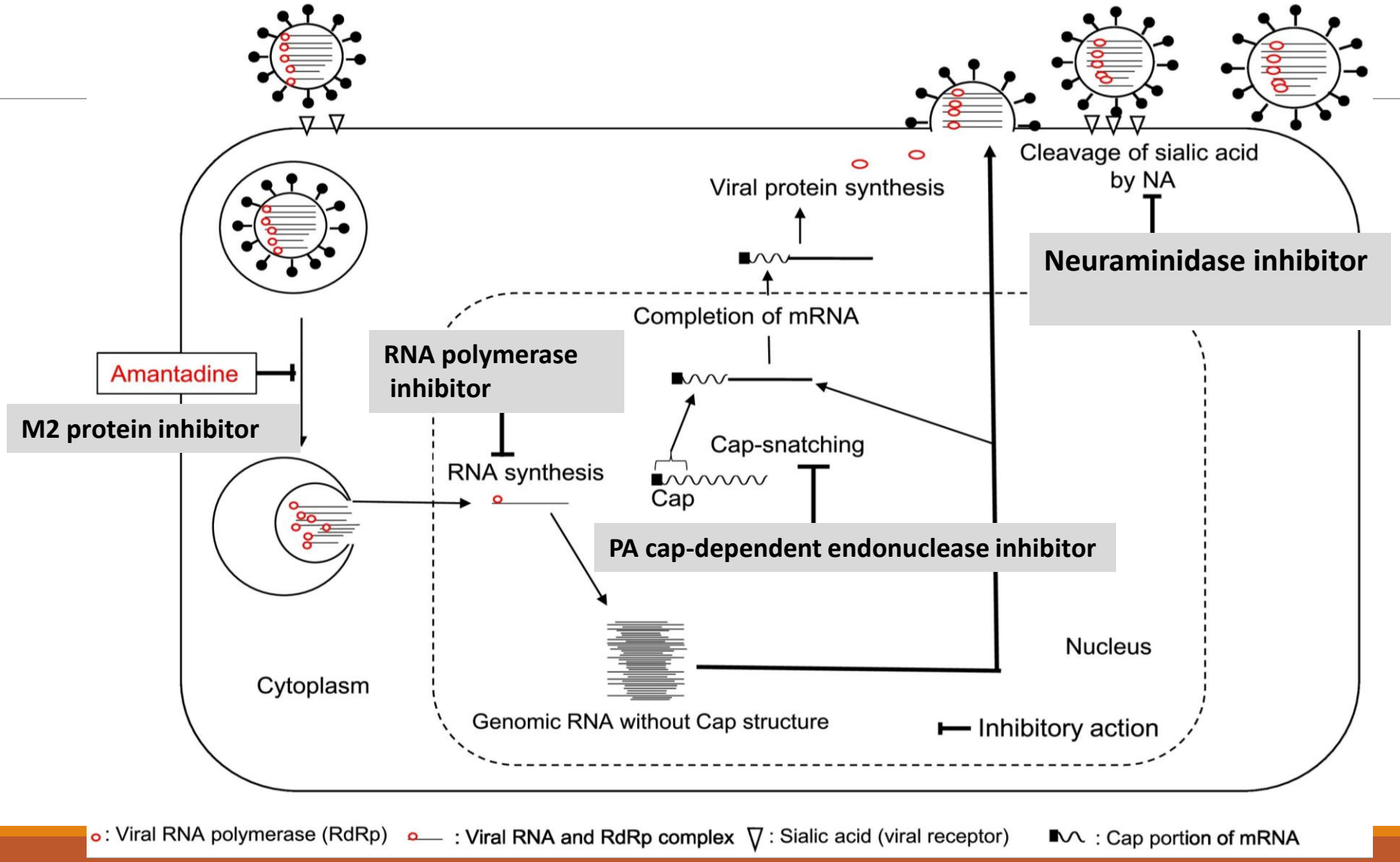
LARS trend through 2026/8/29
CDC press release 2026/9/1

Influenza Virus



Pharmacology & Therapeutics 209(2020)107512

Influenza Virus



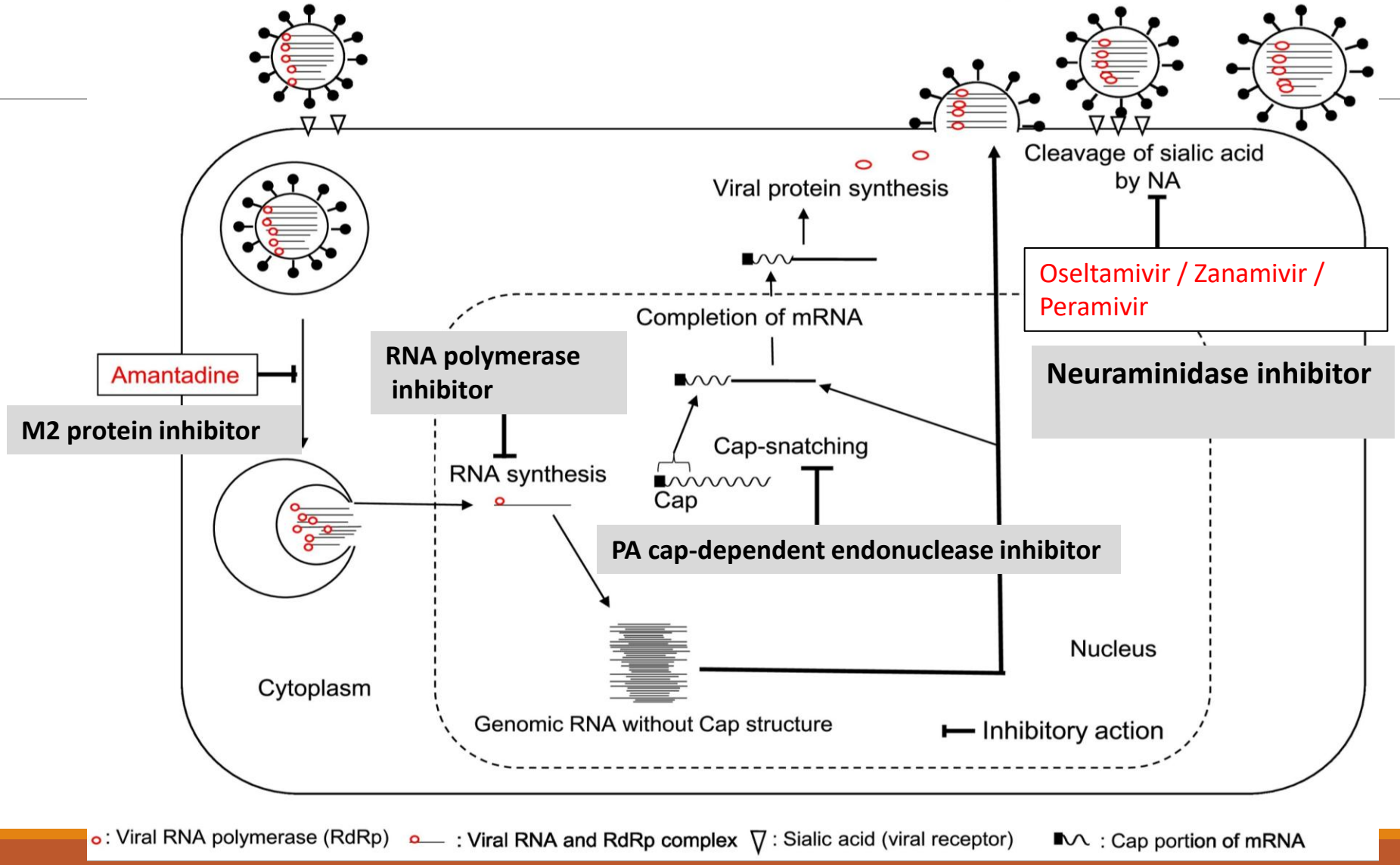
Pharmacology & Therapeutics 209(2020)107512

M2 protein inhibitor

- Mechanism : Inhibit viral uncoating
- Drug : Amantadine／Rimantadine
- Only active against influenza A
- Widespread resistance

已不建議使用於流感病毒感染治療

Influenza Virus- Neuraminidase inhibitor



Neuraminidase inhibitor

- Mechanism : inhibiting viral release
- Drug : Oseltamivir、Zanamivir、
  Peramivir
- Active against influenza A and B

目前抗病毒藥物主流

Neuraminidase inhibitor



克流感(Oseltamivir) PO



瑞樂沙 (Zanamivir) INH



瑞貝塔 (Peramivir) IV

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Cochrane Database of Systematic Reviews

Neuraminidase inhibitors for preventing and treating influenza in adults and children

Cochrane Systematic Review - Intervention | Version publish

https://doi.org/10.1002/14651858.CD008965.pub4

Am score 756 View article information

Tom Jefferson | Mark A Jones | Peter Doshi | Chr
| Igho J Onakpoya | Kamal R Mahtani | David Nuna
View authors' declarations of interest

Time to first symptom alleviation. For the treatment of adults, oseltamivir reduced the time to first alleviation of symptoms by 16.8 hours (95% confidence interval (CI) 8.4 to 25.1 hours, P < 0.0001). This represents a reduction in the time to first alleviation of symptoms from 7 to 6.3 days. There was no effect in asthmatic children, but in otherwise healthy children there was (reduction by a mean difference of 29 hours, 95% CI 12 to 47 hours, P = 0.001). Zanamivir reduced the time to first alleviation of symptoms in adults by 0.60 days (95% CI 0.39 to 0.81 days, P < 0.00001), equating to a reduction in the mean duration of symptoms from 6.6 to 6.0 days. The effect in children was not significant. In subgroup analysis we found no evidence of a difference in treatment effect for zanamivir on time to first alleviation of symptoms in adults in the influenza-infected and non-influenza-infected subgroups (P = 0.53).

Hospitalisations. Treatment of adults with oseltamivir had no significant effect on hospitalisations: risk difference (RD) 0.15% (95% CI -0.78 to 0.91). There was also no significant effect in children or in prophylaxis. Zanamivir hospitalisation data were unreported.

Serious influenza complications or those leading to study withdrawal. In adult treatment trials, oseltamivir did not significantly reduce those complications classified as serious or those which led to study withdrawal (RD 0.07%, 95% CI -0.78 to 0.44), nor in child treatment trials; neither did zanamivir in the treatment of adults or in prophylaxis. There were insufficient events to compare this outcome for oseltamivir in prophylaxis or zanamivir in the treatment of children.

Pneumonia. Oseltamivir significantly reduced self reported, investigator-mediated, unverified pneumonia (RD 1.00%, 95% CI 0.22 to 1.49); number needed to treat to benefit (NNTB) = 100 (95% CI 67 to 451) in the treated population. The effect was not significant in the five trials that used a more detailed diagnostic form for pneumonia. There were no definitions of pneumonia (or other complications) in any trial. No oseltamivir treatment studies reported effects on radiologically confirmed pneumonia. There was no significant effect on unverified pneumonia in children. There was no significant effect of zanamivir on either self reported or radiologically confirmed pneumonia. In prophylaxis, zanamivir significantly reduced the risk of self reported, investigator-mediated, unverified pneumonia in adults (RD 0.32%, 95% CI 0.09 to 0.41); NNTB = 311 (95% CI 244 to 1086), but not oseltamivir.

46 RCTs (OTM 20, ZAN 26)

主要分析2013年前臨床試驗uncomplicated Flu，結論
OTM可縮短病程 16.8hr (ZAN 14.4hr)，無降低住院風險

Cochrane Database Syst Rev. 2014 Apr 10;2014(4):CD008965.

JAMA Internal Medicine | Original Investigation

Evaluation of Oseltamivir Used to Prevent Hospitalization in Outpatients With Influenza

A Systematic Review and Meta-analysis

Ryan Hanula, BSc; Émilie Bortolussi-Courval, NClin; Arielle Mendel, MD, MSc; Brian J. Ward, MSc, MDCM; Todd C. Lee, MD, MPH; Emily G. McDonald, MD, MSc

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Emily G. McDonald, MD, MSc, Medicine, McGill University Health Centre, Office 3E.03, 5252 De Maisonneuve

JAMA Intern Med. doi:10.1001/jamainternmed.2023.0699
Published online June 12, 2023.

RESULTS Of 2352 studies identified, 15 were included. The intention-to-treat infected (ITTi) population was comprised of 6295 individuals with 54.7% prescribed oseltamivir. Across study populations, 53.6% (5610 of 10 471) were female and the mean age was 45.3 (14.5) years. Overall, oseltamivir was not associated with reduced risk of hospitalization within the ITTi population (RR, 0.77; 95% CI, 0.47-1.27; RD, −0.14%; 95% CI, −0.32% to 0.16%). Oseltamivir was also not associated with reduced hospitalization in older populations (mean age ≥65 years: RR, 0.99; 95% CI, 0.19-5.13) or in patients considered at greater risk of hospitalization (RR, 0.90; 95% CI, 0.37-2.17). Within the safety population, oseltamivir was associated with increased nausea (RR, 1.43; 95% CI, 1.13-1.82) and vomiting (RR, 1.83; 95% CI, 1.28-2.63) but not serious adverse events (RR, 0.71; 95% CI, 0.46-1.08).

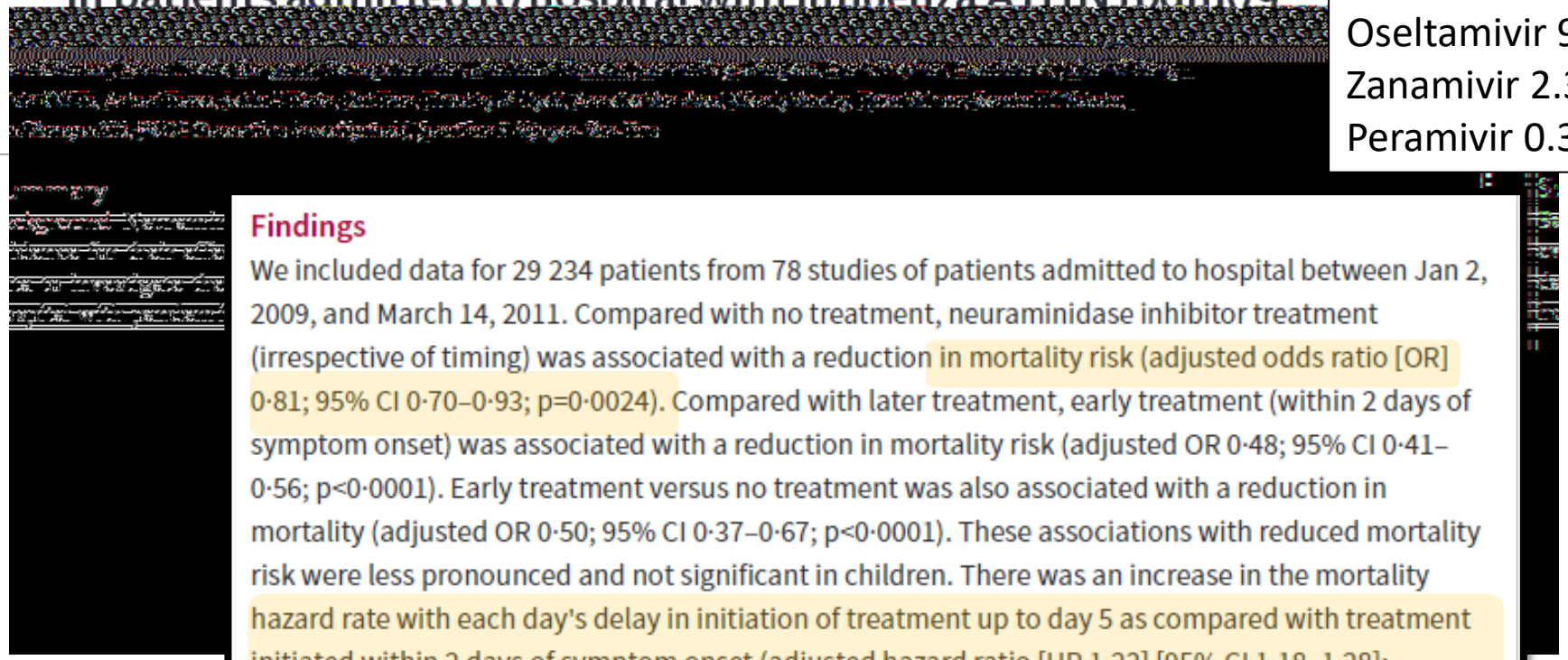
CONCLUSIONS AND RELEVANCE In this systematic review and meta-analysis among influenza-infected outpatients, oseltamivir was not associated with a reduced risk of hospitalization but was associated with increased gastrointestinal adverse events. To justify continued use for this purpose, an adequately powered trial in a suitably high-risk population is justified.

統合分析1999-2020年間15 RCT, outpatients
結果顯示 克流感(OTM)使用無降低住院風險

JAMA Intern Med . 2024 Jan 1;184(1):18-27.

Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09

Oseltamivir 92%
Zanamivir 2.3%
Peramivir 0.3%



Findings

We included data for 29 234 patients from 78 studies of patients admitted to hospital between Jan 2, 2009, and March 14, 2011. Compared with no treatment, neuraminidase inhibitor treatment (irrespective of timing) was associated with a reduction in mortality risk (adjusted odds ratio [OR] 0·81; 95% CI 0·70–0·93; p=0·0024). Compared with later treatment, early treatment (within 2 days of symptom onset) was associated with a reduction in mortality risk (adjusted OR 0·48; 95% CI 0·41–0·56; p<0·0001). Early treatment versus no treatment was also associated with a reduction in mortality (adjusted OR 0·50; 95% CI 0·37–0·67; p<0·0001). These associations with reduced mortality risk were less pronounced and not significant in children. There was an increase in the mortality hazard rate with each day's delay in initiation of treatment up to day 5 as compared with treatment initiated within 2 days of symptom onset (adjusted hazard ratio [HR 1·23] [95% CI 1·18–1·28]; p<0·0001 for the increasing HR with each day's delay).

觀察性研究統合分析近3萬名在2009年H1N1流感大流行期間住院的病人，發現流感住院病人服用抗病毒藥劑能降低死亡風險有關

Lancet Respir Med. 2014;2(5):395-404.

SURVEILLANCE

Effect of neuraminidase inhibitor (oseltamivir) treatment on outcome of hospitalised influenza patients, surveillance data from 11 EU countries, 2010 to 2020

Cornelia Adlhoch[1], Concepción Delgado-Sanz[2], AnnaSara Carnahan[3], Amparo Larrauri[2], Odette Popovici[4], Nathalie Bossuyt[5], Isabelle Thomas[5], Jan Kynčl[6], Pavel Slezak[6], Mia Brytting[3], Raquel Guiomar[7], Monika Redlberger-Fritz[8], Jackie Maistre Melillo[9], Tanya Melillo[9], Arianne B. van Gageldonk-Lafeber[10], Sierk D. Marbus[10], Joan O'Donnell[11], Lisa Domegan[11], Joana Gomes Dias[1],

TABLE 2

Risk of death in hospitalised influenza cases by age group, sex, influenza subtype, timing of antiviral treatment, care unit admission status, timing of hospitalisation and vaccination status, 11 European Union countries, influ 2010/11–2019/20

Variable	0–19 years		20–39 years		40–59 years		60–79 years		
	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI	aO
Female sex	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref
Male sex	0.81	0.45–1.46	1.16	0.73–1.83	1.06	0.84–1.33	1.16[a]	1.00–1.33	1.0
Influenza virus									
								5–1.45	1.1
								3–1.14	1.0
								6–0.99	0.8
								9–0.63	0.5
								1–0.65	0.6
								7–0.75	0.6
								1–1.41	0.7
								Ref.	Ref
								6–4.78	1.4
								8–0.94	0.9
								Ref.	Ref
								1–1.22	0.9

ntensive care

p<0.001.

歐盟多國觀察性研究分析近2萬名在2009/2010及2019/2020年流感流行期間住院的病人
發現(越早)服用Oseltamivir能降低死亡風險有關

Euro Surveill . 2023 Jan;28(4):2200340.

ERJ open research

Early oseltamivir treatment improves survival in critically ill patients with influenza pneumonia

Gerard Moreno[1,15], Alejandro Rodríguez[1,15], Jordi Sole-Violán[2], Ignacio Martín-Loeches[3], Emili Díaz[4], María Bodí[1], Luis F. Reyes[5], Josep Gómez[1], Juan Guardiola[6], Sandra Trefler[1], Loreto Vidaur[7], Elisabet Papiol[8], Lorenzo Socias[9], Carolina García-Vidal[10], Eudald Correig[1], Judith Marín-Corral[11], Marcos I. Restrepo[12], Jonathan S. Nguyen-Van-Tam[13] and Antoni Torres[14] on behalf of the GETGAG Working Group[16]

Background: The relationship between early oseltamivir treatment (within 48 h o mortality in patients admitted to intensive care units (ICUs) with severe influenza aimed to investigate the association between early oseltamivir treatment and ICU m patients with influenza pneumonia.

Methods: This was an observational study of patients with influenza pneumonia ad Spain during 2009–2018. The primary outcome was to evaluate the association bet treatment and ICU mortality compared with later treatment. Secondary outcomes

duration
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Results
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Conclus
with inf

西班牙多中心ICU觀察性研究2124位流感重症病人,early oseltamivir使用跟降低ICU住院風險、ICU留滯天數及呼吸器使用天數有關

ERJ Open Res. 2021;7(1):00888-2020.

Open Forum Infectious Diseases

MAJOR ARTICLE

Efficacy and Safety of Intravenous Peramivir Compared With Oseltamivir in High-Risk Patients Infected With Influenza A and B Viruses: A Multicenter Randomized Controlled Study

Shigeki Nakamura,[1,6] Taiga Miyazaki,[1,2] Koichi Izumikawa,[2] Hiroshi Kakeya,[3] Yutaka Saisho, Katsunori Yanagihara, Yoshitsugu Miyazaki,[6] Hiroshi Mukae,[1] and Shigeru Kohno[1]

[1]Department of Respiratory Diseases, Nagasaki University Hospital, [2]Department of Infectious Diseases, Nagasaki University Graduate School of Biomedical Sciences, [3]Department of Infection Control Science, Graduate School of Medicine, Osaka City University, [4]Medical Affairs, Shionogi & Co, Ltd, Osaka, [5]Department of Laboratory Medicine, Nagasaki University Graduate School of Biomedical Sciences, and [6]Department of Chemotherapy and Mycoses, National Institute of Infectious Diseases, Tokyo, Japan

Background. Clinical studies comparing the different neuraminidase inhibitors for treatment of at-risk patients with influen have not been performed. To optimize such treatments, we assessed the efficacy and safety of intravenous peramivir compared wi oral oseltamivir in treating seasonal influenza A or B virus infection.

Methods. A multicenter, randomized, controlled clinical trial was conducted from December 2012 to May 2014 in high-ri patients infected with seasonal influenza. A total of 92 adult inpatients and outpatients with high risk factors (HRFs) were treat by either a single intravenous infusion of peramivir (600 mg) or oral administration of oseltamivir (75 mg, twice per day for 5 day

Results. The median times to clinical stability (time to reach <37°C) were 40.0 hours (95% confidence interval [CI] = 23.3–64 and 37.8 hours (95% CI = 26.3–45.3) in the peramivir and oseltamivir groups, respectively; these values did not reveal a significa difference. The virus titer and change of mean total symptom scores decreased similarly with both treatments. Results of step-w regression suggested that virus type was a significantly effective prognostic factor with respect to illness resolution. Adverse ever (AEs) with peramivir and oseltamivir occurred in 2.2% (n = 1/46) and 13.0% (n = 6/46) of patients, respectively. The severity of A

IV peramivir：方便 ≠ superiority

Meta-analysis

Comparing intravenous peramivir with oral oseltamivir for patients with influenza: a meta-analysis of randomized controlled trials

Yu-Hsing Fang, Tzu-Herng Hsu, Tzu-Yin Lin, Chia-Hung Liu, Shou-Chu Chou, Jie-Ying Wu & ...show all

Pages 1039-1046 | Received 21 Oct 2020, Accepted 15 Jan 2021, Published online: 01 Mar 2021

Download citation https://doi.org/10.1080/14787210.2021.1878025 Check for updates

Results

The meta-analysis was conducted to calculate the pooled effect size by using a random-effects model. Seven randomized controlled trials (RCTs) including 1,138 patients were reviewed. The incidence of total complications revealed no significant difference between 600 mg IV peramivir (P600) and 75 mg oral oseltamivir (O75) treatments (2.8% vs. 4.1%; risk ratio [RR] = 0.70; 95% confidence interval [CI]: 0.36–1.38). The incidence of pneumonia was not significantly different between the P600 and O75 treatment groups (2.2% vs. 2.7%; RR = 0.74; 95% CI: 0.37–1.51). Regarding the time to the alleviation of symptoms, no difference was found in P600 and O75 treatment (MD = −3.00; 95% CI: −11.07 to 5.06). The rate of fever clearance in 24 h and the time to fever resolution were not statistically different between the IV peramivir and oral oseltamivir treatments (at different dosages) groups.

RCT證據顯示在high risk急門診流感病人使用oseltamivir或peramivir治療，兩者退燒時間及病毒量下降變化無差異

7 RCT的MA ：complications、pneumonia、symptoms、fever outcomes 無差異

Open Forum Infect Dis. 2017;4(3):ofx129.

Expert Rev Anti Infect Ther. 2021;19(8):1039-1046.

Neuraminidase inhibitors 實證結論

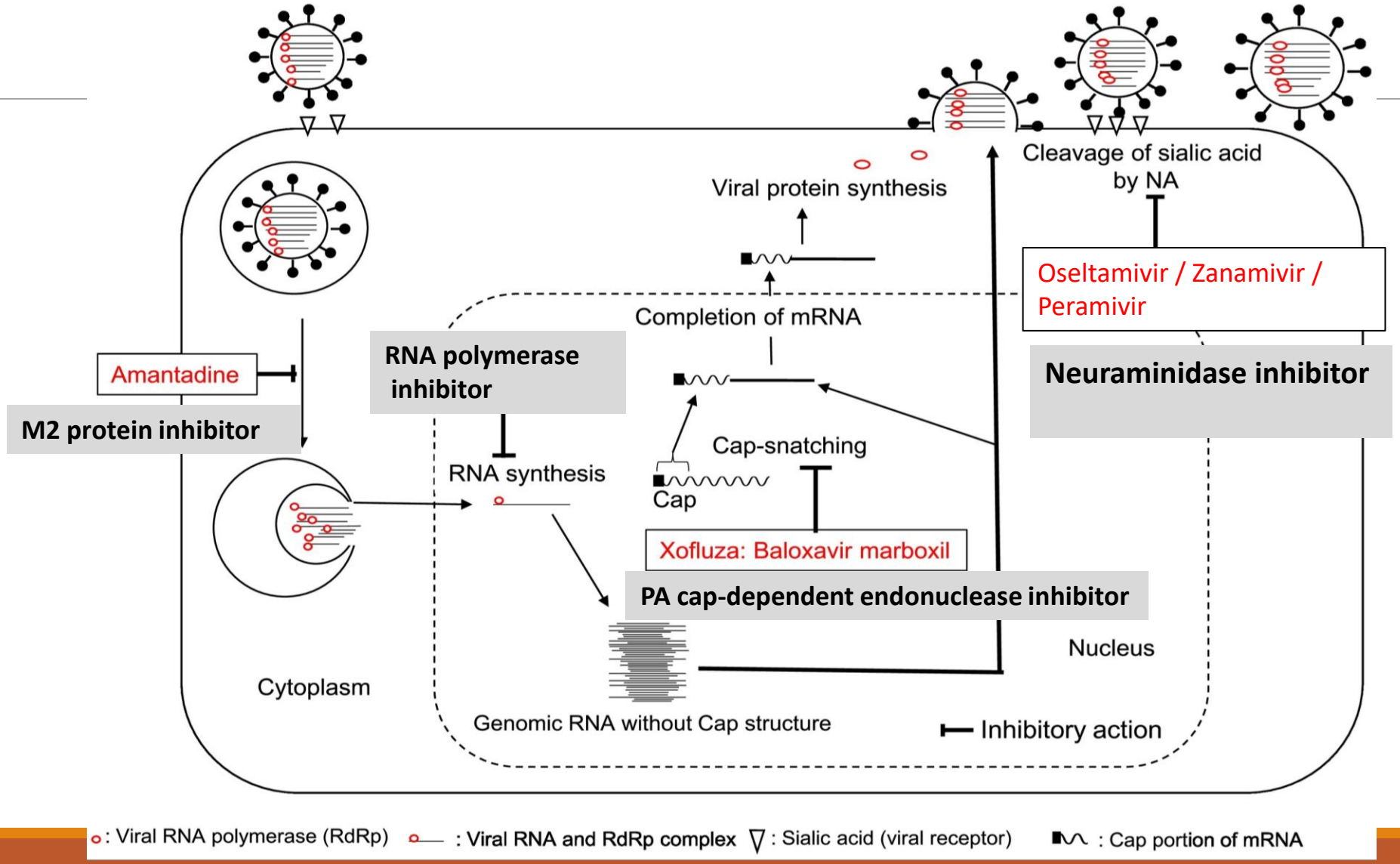
	克流感/易剋冒 (Oseltamivir)	瑞樂沙 (Zanamivir)	瑞貝塔 (Peramivir)

台灣 CDC :符合公費條件者不需等待快篩即可及早給藥，目的為減少嚴重併發症及死亡；也指出 48 小時內效果最好、超過 48 小時仍可能有效。

美國 CDC 也仍建議 hospitalized flu 儘快給 oseltamivir

實證顯示針對易併發重症之高風險對象（老人、幼兒、慢性疾病、孕婦），不論發病時間，均應立刻給予抗病毒藥物治療，以降低死亡風險

Influenza Virus- endonuclease inhibitor



Endonuclease inhibitor

- Mechanism : inhibiting the initiation of mRNA synthesis
- Drug : Baloxavir (*single dose* oral dose)

Active against influenza A and B

潛在抗病毒藥物主流



Baloxavir

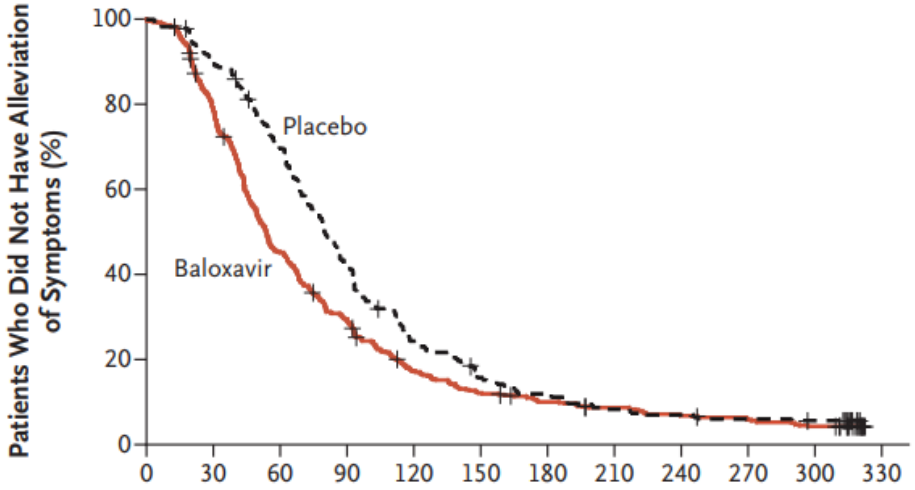
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 6, 2018 VOL. 379 NO. 10

Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents

Frederick G. Hayden, M.D., Norio Sugaya, M.D., Nobuo Hirotsu, M.D., Ph.D., Nelson L

CAPSTONE-1 study



隨機分派研究證據顯示在健康成人與placebo相比可縮短臨床症狀(53.7小時 vs 80.2小時)及更快降低 viral titer 與oseltamivir相比更快降低 viral titer(24小時 vs 72小時)

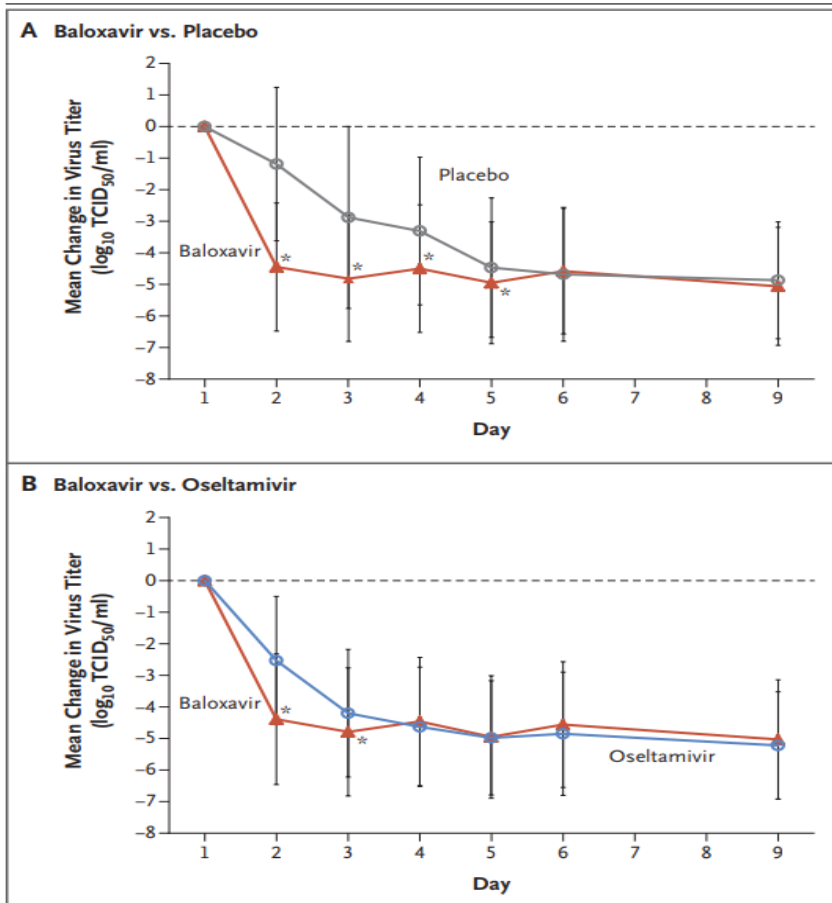


Figure 3. Change from Baseline in Influenza Infe

N Engl J Med. 2018;379(10):913-23

Early treatment with baloxavir marboxil in high-risk adolescent and adult outpatients with uncomplicated influenza (CAPSTONE-2): a randomised, placebo-controlled, phase 3 trial

CAPSTONE-2 study

Michael G Ison, Simon Portsmouth, Yuki Yoshida, Takao Shishido, Melissa Mitchener, Kenji Tsuchiya, Takeki Uehara, Frederick G Hayden

Summary

oxil (hereafter baloxavir), a selective inhibitor of influenza cap-dependent endonuclease, ne USA and Japan for the treatment of uncomplicated influenza in otherwise healthy d older. We aimed to study the efficacy of baloxavir in outpatients at high risk of developing cations.

enrolled from Jan 11, 2017, to March 30, 2018, and r oseltamivir (n=725). The modified intention-to-treat population included 1163 patients: 386 in the placebo group, and 389 in the oseltamivir group. 557 (48%) of 1163 patients had %) had influenza B, 80 (7%) had influenza A H1N1, 14 patients had a mixed infection, and -typable viruses. The median TTIIS was shorter in the baloxavir group (73·2 h [95% CI acebo group (102·3 h [92·7 to 113·1]; difference 29·1 h [95% CI 14·6 to 42·8]; p<0·0001). seltamivir group was 81·0 h (95% CI 69·4 to 91·5), with a difference from the baloxavir ·7). Adverse events were reported in 183 (25%) of 730 patients in the baloxavir group, cebo group, and 202 (28%) of 721 in the oseltamivir group. Serious adverse events were bal erte side onfe stit alox n-ris early therapy for patients at high

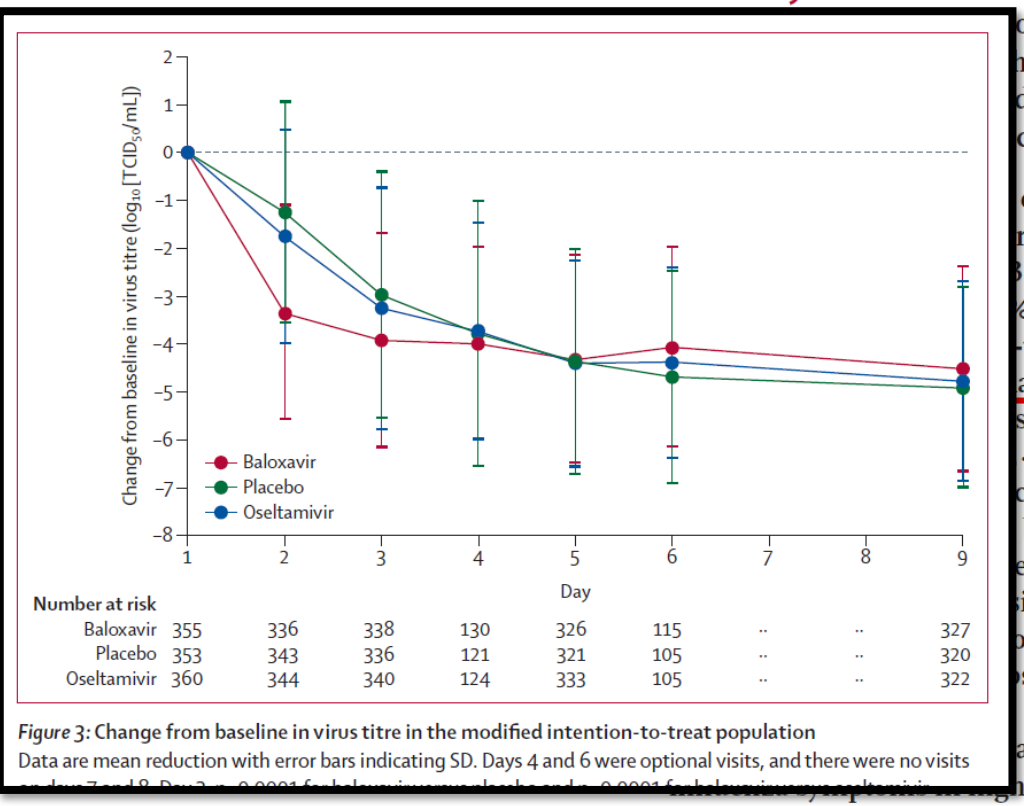


Figure 3: Change from baseline in virus titre in the modified intention-to-treat population
Data are mean reduction with error bars indicating SD. Days 4 and 6 were optional visits, and there were no visits

Influenza B subgroup：Baloxavir 的 symptom improvement 優於 oseltamivir，差距 27 h。

隨機分派研究證據顯示在高風險族群與placebo相比可縮短臨床症狀(73.2小時 vs 102.3小時)及更快降低 viral titer
與oseltamivir相比更快降低 viral titer

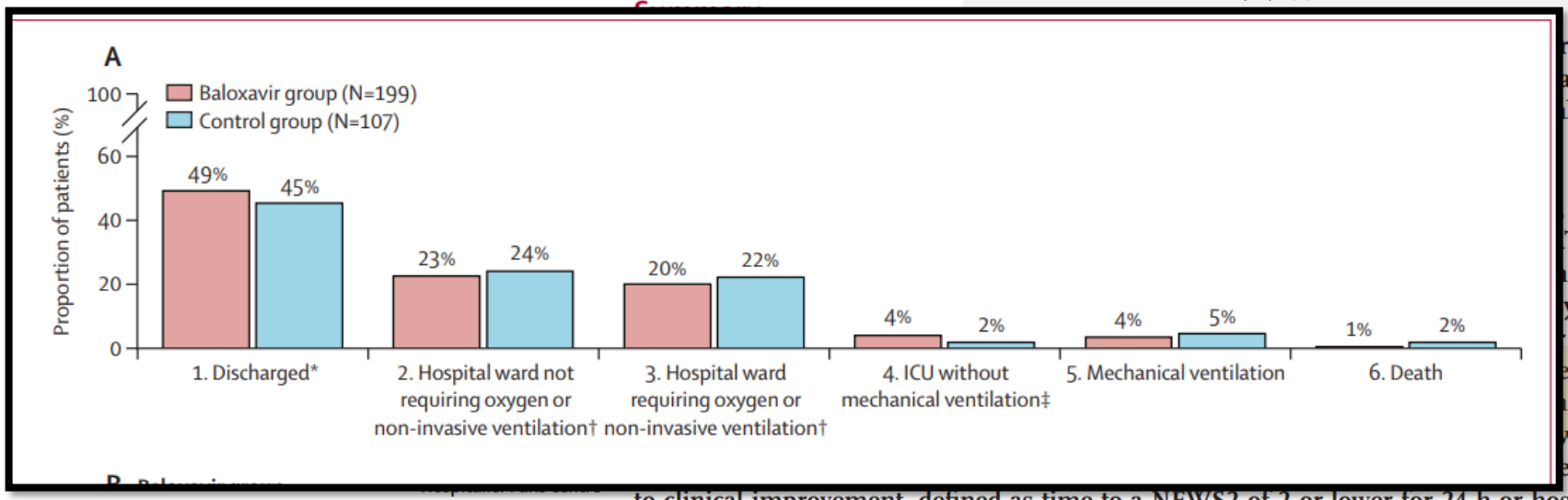
Lancet Infect Dis. 2020;20(10):1204-1214.

Combining baloxavir marboxil with standard-of-care neuraminidase inhibitor in patients hospitalised with severe influenza (FLAGSTONE): a randomised, parallel-group, double-blind, placebo-controlled, superiority trial

FLAGSTONE study

Deepali Kumar, Michael G Ison, Jean-Paul Mira, Tobias Welte, Jick Hwan Ha, David S Hui, Nanshan Zhong, Takefumi Saito, Laurie Katugampola, Neil Collinson, Sarah Williams, Steffe

Baloxavir治療劑量 on D1,D4 +/- D7



re for hospitalised patients with ase inhibitor baloxavir marboxil l outcomes compared with NAI

superiority trial. Patients aged T-PCR or a rapid test) and had a t took place in 124 centres across ystem, patients were randomly placebo plus NAIs (hereafter the ed to group assignment. Baloxavir g for ≥80 kg), and on day 7 if no were oseltamivir, zanamivir, and e. The primary endpoint was time to clinical improvement, defined as time to a NEWS2 of 2 or lower for 24 h or hospital discharge, whichever came first, based o The modified received a do assigned at r least one dos registered wi

Université de Paris, Cochin University Hospital, Medical Intensive Care Unit, Paris, France (Prof J-P Mira MD); Department of Pneumology and German Centre of Lung Research (DZL), Hannover Medical School, Hannover, Germany (Prof T Welte MD);

隨機分派研究證據顯示在流感重症病人
baloxavir合併NAIs與NAIs相比, 臨床預後相當
但NAIs合併baloxavir可降 viral RNA 更快

Lancet Infect Dis. 2022;22(5):718-730.

Treatment evidence before entering resistance

- 目前主流抗病毒藥物有：口服Oseltamivir五天、吸入劑Zanamivir五天、針劑Peramivir單次、口服Baloxavir單次

1. Uncomplicated influenza：antivirals shorten illness modestly.
2. NAI 對於住院病人, 有觀察型研究發現跟較低死亡風險有關
3. Baloxavir has faster virologic activity than oseltamivir.
4. Influenza B is one setting where baloxavir has comparatively favorable evidence.
5. Routine combination therapy is not supported.

https://www.cdc.gov/flu/professionals/antivirals/summary-clinicians.htm

Outline

- 抗流感病毒藥物機轉及實證
- 流感藥物治療建議及實證更新
- 抗流感病毒藥物抗藥性現況

流感病人治療國內外指引共識

- 非屬重症高風險或高傳播族群之輕症病患，以**支持性療法**為主。大多數人可自行痊癒，而不需使用抗病毒藥物

- **易併發重症之高風險對象**，出現危險徵兆者或重症住院病患，不需等待確診，不論發病時間，均應立刻給予抗病毒藥物治療（NAIs, Baloxavir）
- 住院或重症病人應及早給予抗病毒治療；目前多數指引對 hospitalized/severe influenza 仍以 oseltamivir-based therapy 為主。

高危險族群：
2歲以下幼兒
65歲以上老人
慢性疾病 (心血管疾病、肺部疾病、糖尿病、肝腎疾病)
免疫功能不全 (移植及癌症及HIV病人)
孕婦或最近兩週內生產的產婦
病態肥胖

JAMA. 2009;302(17):1896-1902.

公費流感抗病毒藥劑使用對象一覽表

全年適用

除法定傳染病外，應為本國籍人士或持有居留證
【18歲(含)以下孩童其父母需一方為本國籍或持有居留證】

治療性用藥條件 經醫師評估符合條件者，無須快篩即可用藥

法定傳染病

需通報於法定傳染病通報系統及填寫法傳編號

- 「流感併發重症」通報病例
- 「新型A型流感」通報病例

住院病患

- **確診或疑似罹患流感住院(含急診待床)之病患**
  罹患流感因病況嚴重而需住院治療的病患，並不包括門診病人，依此條件使用公費藥劑者須備有「住院紀錄」或「急診待床紀錄」

門急診病患

- **未滿5歲及65歲以上之類流感患者**
- **孕婦及產後兩週內之婦女經評估需及時用藥者**
  領有國民健康署核發孕婦健康手冊之婦女
- **肥胖之類流感患者(BMI≧30或未滿18歲兒童青少年BMI超過同齡第95百分位)**
  未滿18歲兒童青少年BMI第95百分位一覽表詳如附件
- **具重大傷病、免疫不全(含使用免疫抑制劑者)或流感高風險慢性疾病之類流感患者**
  1.重大傷病：IC卡註記為重大傷病或持有重大傷病證明紙卡者
  2.流感高風險慢性疾病之ICD CODE：B20 , Z21 , D80-84 , D86 , D89 , E08-13 , E66 , E85 , G09 , G20 , G30-32 , G35-37 , G40 , G45-46 , G65 , G70 , G72 , I00-02 , I05-09 , I11-13 , I20-22 , I24-25 , I27-28 , I34-37 , I42-43 , I44-45 , I47-49 , I50-51 , I60-62 , I63 , I67-69 , I70 , I71, I72 , I73-74 , I77 , I79 , J40-45 , J47 , J60-70 , J82 , J84 , J96 , J98 , J99 , K70-72 , K73-76 , B18-19 , M05-06 , M30-31 , M32-34 , M35 , M94.1 , N00-01 , N03 , N05 , N04 , N18-19 , N26-27 , Q89.01 , Z90.81

預防性用藥條件

需通報衛生局進行疫情調查，並經疾病管制署各區管制中心防疫醫師或傳染病防治醫療網區正/副指揮官或其授權人員同意後始可用藥

需通報並經審核

- **類流感等群聚事件經疾病管制署各區管制中心防疫醫師認定需用藥者**
  需填寫群聚編號
- **「新型A型流感」極可能/確定病例之密切接觸者**
  接觸者名冊經傳染病防治醫療網區正/副指揮官或其授權人員研判需給藥者;需填寫所接觸之個案的法傳編號
- **動物流感發生場所撲殺清場工作人員**
  接觸者名冊經傳染病防治醫療網區正/副指揮官或其授權人員研判需給藥者；需填寫禽畜場名稱或編號

流感高峰期

擴大用藥條件

- **有類流感症狀，且具下列身分之流感高傳播族群：115年8月24日至115年9月30日**

1. 醫事單位之防疫相關人員(含具執業登記醫事人員及醫療院所非醫事人員)
2. 安養、長期照顧(服務)等機構之受照顧者及所屬工作人員
3. 幼兒園托育人員、托育機構專業人員及居家托育人員(保母)
4. 幼兒園、國小、國中、高中、高職、五專1至3年級學生
5. 與流感重症高風險族群同住或其照顧者
6. 禽畜養殖等相關行業工作人員、動物園工作人員及動物防疫人員
7. 其他人口密集機構(如軍營等)易發生群聚之人員

流感預防性用藥

藥物	PEP適應症/劑量	關鍵實證發現	文獻
Oseltamivir(PO)	家戶接觸者:75mg QD×10天(或依社區/機構暴露延長)	隨機安慰劑對照試驗顯示可降低有症狀流感風險達68-89%; **高風險族群48hrs給藥**RR=0.4	1. JAMA. 2001;285;(6):748-754 2. Lancet. 2024. Zhao Y, Gao Y, Guyatt G, et al (**WHO Systemic review+MA (33 RCT, n=19,096)**)
Zanamivir(INH)	家戶接觸者:**2 inhalations QD×10天**	隨機安慰劑對照試驗顯示保護效力達82-84% **高風險族群48hrs給藥**RR=0.35	1. NEJM 2000. Hayden FG, Gubareva LV, Monto AS, et al.. 2. Lancet. 2024. Zhao Y, Gao Y, Guyatt G, et al
Baloxavir marboxil(PO)	家戶接觸者: **單劑**,適用於≥5歲	多中心RCT(752名家戶接觸者):aHR=0.14,保護效力約86%;對高風險族群、兒童、未接種疫苗者均有效; **高風險族群48hrs給藥**RR=0.43 治療index case, Day5相對傳染風險降低29%	1. N Engl J Med 2020; 383:309-320 2. Lancet. 2024. Zhao Y, Gao Y, Guyatt G, et al 3. N Engl J Med 2025;392:1582-1593
Peramivir(IV)	無PEP適應症	無相關試驗數據	

Chemoprophylaxis is selective - not routine

項目	台灣 CDC	美國 CDC
一般家庭接觸者	**不常規**公費預防性投藥	**不建議** routine PEP；可密切監測症狀，必要時及早治療
流行期擴大公費用藥	是治療 symptomatic ILI，不是 prophylaxis	無對應政策
長照/機構群聚	高風險接觸者可依公衛評估申請 prophylaxis	建議暴露住民 chemoprophylaxis
新型 A 型流感接觸者	可公費 prophylaxis	高風險建議PEP
可用藥物	**Oseltamivir、Zanamivir（公費主體）**	**Oseltamivir、Zanamivir、Baloxavir**
Peramivir	不作常規 prophylaxis	Not recommended
建議時間	**10天**依公衛事件/群聚處置原則	**一般暴露後 7 天**
機構群聚療程	依 CDC 群聚處置流程	至少 2 週，且持續到最後病例後 7 天

非重症門診：抗病毒有效，但 patient-important benefit 不大

2025 network meta-analysis | 73 RCTs | 34,332 outpatients

JAMA Internal Medicine | Original Investigation

Antiviral Medications for Treatment of Nonsevere Influenza

A Systematic Review and Network Meta-Analysis

Outcome	Baloxavir	Oseltamivir
高風險住院 risk difference	**−1.6%** (−2.0 to +0.4) Low certainty	**−0.4%** (−1.0 to +0.4) High certainty
Time to symptom alleviation	**−1.02 days** Moderate certainty	**−0.75 days** Moderate certainty
Treatment-related adverse events	**−3.2%** **High certainty**	**+2.8%** **Moderate certainty**

怎麼解讀

- 死亡/住院 event rate 很低，很多 trial 本來就 underpowered
- Baloxavir 對高風險住院 benefit 是 low certainty

跟Placebo的結果：低風險健康成人可 shared decision；不要把這篇外推成「高風險/住院不用治療」。

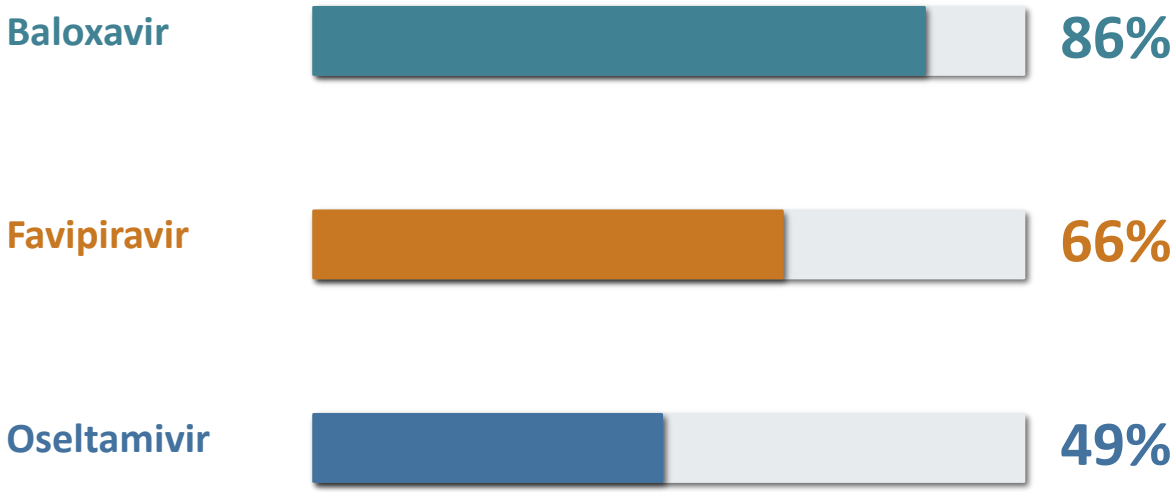
Gao Y et al. JAMA Intern Med. 2025;185:293–301.

AD ASTRA：Baloxavir 病毒學效力最強

但 viral RNA clearance ≠ clinical outcome

Baloxavir marboxil, favipiravir, or oseltamivir in patients with non-severe symptomatic seasonal influenza (AD ASTRA): a phase 2, open-label, adaptive, randomised controlled trial

Viral clearance acceleration vs no study drug



What actually changed clinically?

0.5–0.9 d
Fever resolution
faster vs control

No clear Δ
All symptoms
between groups

Design limitations

- **18–60 歲、低風險**
- open-label
- primary endpoint = oropharyngeal viral RNA
- not powered for severe outcomes

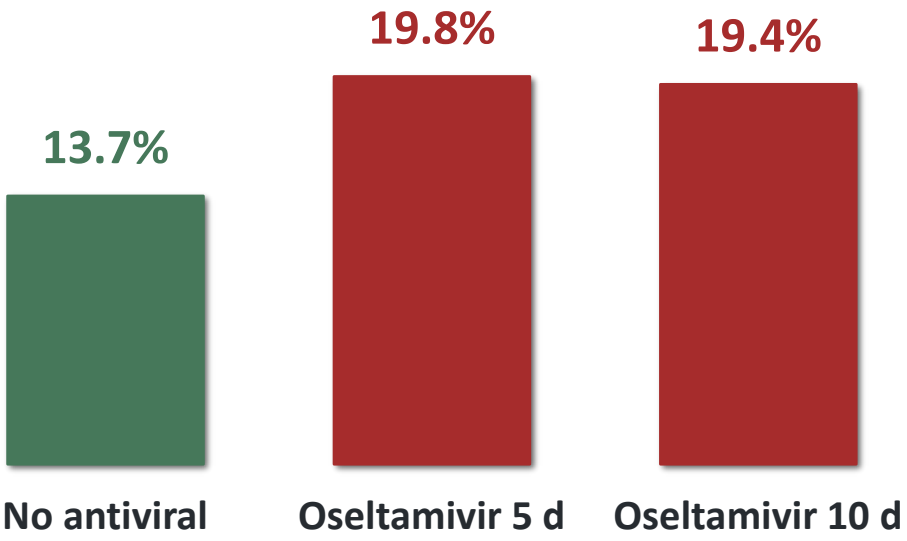
Baloxavir 把病毒量打得最快；這不等於已證明能減少住院或死亡。

Jittamala P et al. Lancet Infect Dis. Published online 2026-07-28 (AD ASTRA).

REMAP-CAP：organ-support ICU 出現不利於 Oseltamivir 的死亡訊號

Preprint • not yet formally peer reviewed

90-day mortality



Baloxavir ± oseltamivir arms are not reported; evaluation ongoing.

Oseltamivir for Critically Ill Patients with Influenza: A Randomised Trial

29 Pages • Posted: 27 Jul 2026

Preprints with THE LANCET

Trial population

n = 442 • age ≥12 • confirmed influenza
HFNC/NIV/IMV or vasopressors

aOR 2.13	aOR 2.17
5-day vs none	10-day vs none
95% CrI 1.03–4.52	95% CrI 1.05–4.64

Posterior P(harm): 98.0% / 98.2%

Adaptive inferiority threshold crossed → oseltamivir arms stopped.

10

REMAP-CAP Investigators. Oseltamivir for Critically Ill Patients with Influenza. 2026 preprint

REMAP-CAP：8.9% crossover 到底是什麼？

8.9% crossover

被 randomize 到 no-antiviral 的 124 人中，約 11 人在 randomization 後仍收到 ≥1 dose oseltamivir。

Primary analysis 仍依 ITT 留在 no-antiviral group

對結果的方向

若 oseltamivir 真的有害，control arm 的 crossover 理論上會把兩組拉近，較像 bias toward the null，而不是製造 harm signal。

小心解讀caveats

- Open-label：病人與 clinical team 知道分組
- 41.8% 在 randomization 前已接受 1 dose oseltamivir
- no-antiviral option 僅 79 / 139 sites 提供; potential site-level confounding
- **per-protocol 仍同方向：aOR 1.87 / 1.81，但 credible interval 跨 1**
- 不能外推到低風險門診、高風險門診、一般住院但尚未 organ support

REMAP-CAP Investigators. Oseltamivir for Critically Ill Patients with Influenza. 2026 preprint

誰要立即治療？基本框架沒有變；可能變的是 critical illness

住院	重症 / progressive	高風險門診	健康低風險門診
立即 empiric antiviral 不要等確認	即使 >48 h 仍通常治療 但 critical illness 現在有爭議	盡早治療 不等待 confirmation	≤48 h 可 shared decision

CDC 2026.03	Hospitalized suspected/confirmed influenza → oral/enteric oseltamivir ASAP.
Australian Living Evidence 2026.08	Critically ill adults：strong recommendation against oseltamivir.

不要把「critically ill」的新訊號外推到所有住院病人。

Combination、high dose、延長療程：routine 都不建議

CDC Summary for Clinicians 2026; Australian Living Evidence Collaboration interim influenza guideline 2026.

Outline

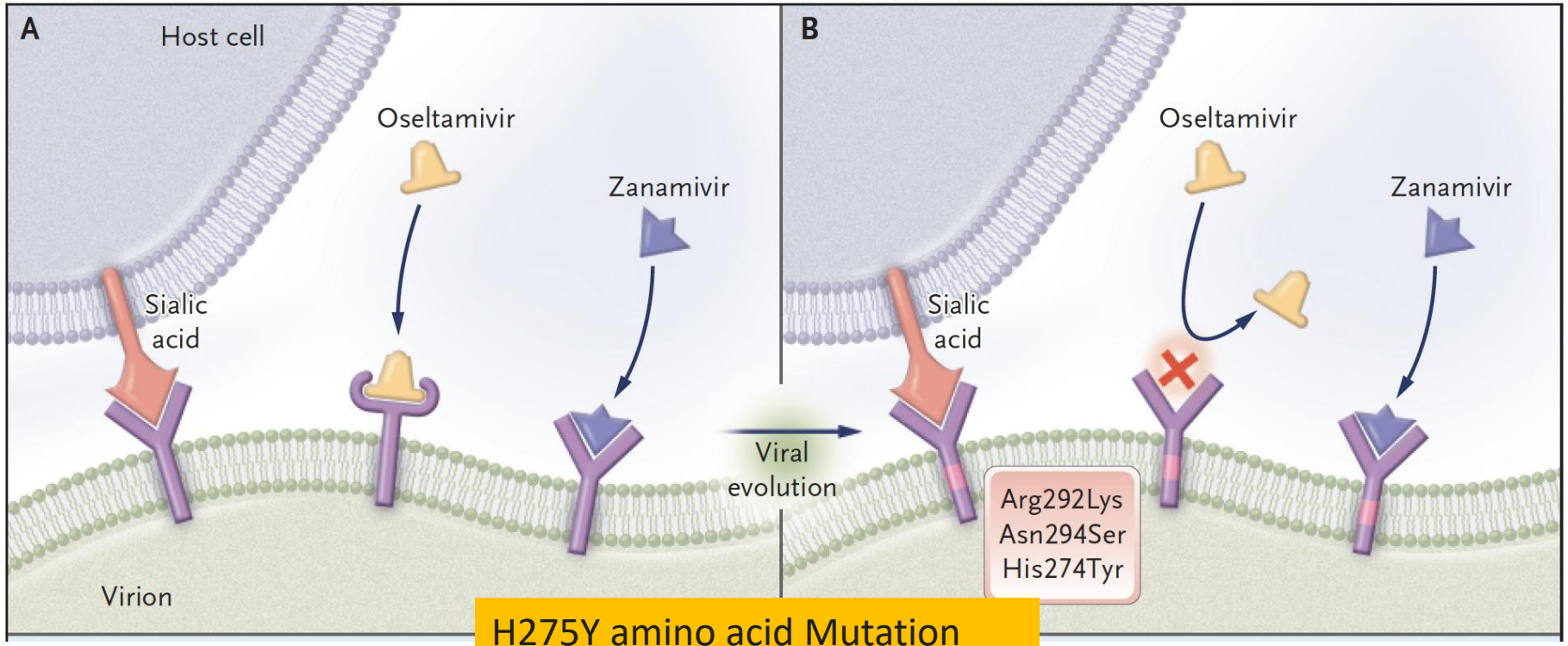
- 抗流感病毒藥物機轉及實證
- 流感藥物治療建議及實證更新
- 抗流感病毒藥物抗藥性現況

警鐘響起—NAI抗藥性

- 病毒基因突變：**H275Y** amino acid Mutation. His274Tyr, Arg292Lys, Asn294Ser，改變病毒與NAI 結合部位，使得oseltamivir不易與neuraminidase active site結合

- 病毒突變株並不會降低病毒的生存能力(fitness)及傳染力(transmissibility)

- 2007-2008 H1N1流行於北半球的病毒株帶有神經胺酸酶突變的比例為10%~70%, 2008-2009年美國舊seasonH1N1突變比例高達98%



H275Y amino acid Mutation

N Engl J Med 2009; 360:953-6

抗藥性：台灣與美國的抗藥性整體仍低

Cross-resistant to peramivir

Taiwan CDC

Period / target	H1N1	H3N2	B
2024–25 season Oseltamivir resistance	59 / 780 7.6%	0 / 234	0 / 179
2025–26 early season NAI resistance (to wk45)	0 / 7	0 / 33	0 / 1

Taiwan CDC 2025/9/29：2025 calendar-year 約 6.5% H1N1 帶 oseltamivir/peramivir resistance-associated mutation；H3/B 未見；Baloxavir 各型別未見 resistance mutation。

US CDC 2025–26 full season

Drug	Tested	Reduced / decreased	Highly reduced
Oseltamivir	4,609	20 (0.4%)	11 (0.2%)
Peramivir	4,609	3 (0.1%)	9 (0.2%)
Zanamivir	4,609	0	0
Baloxavir	4,491	0	—

Key point：population-level resistance 仍低；但 H1N1 是 NAI resistance 最需要盯的 subtype。

什麼時候真的要懷疑抗藥性？

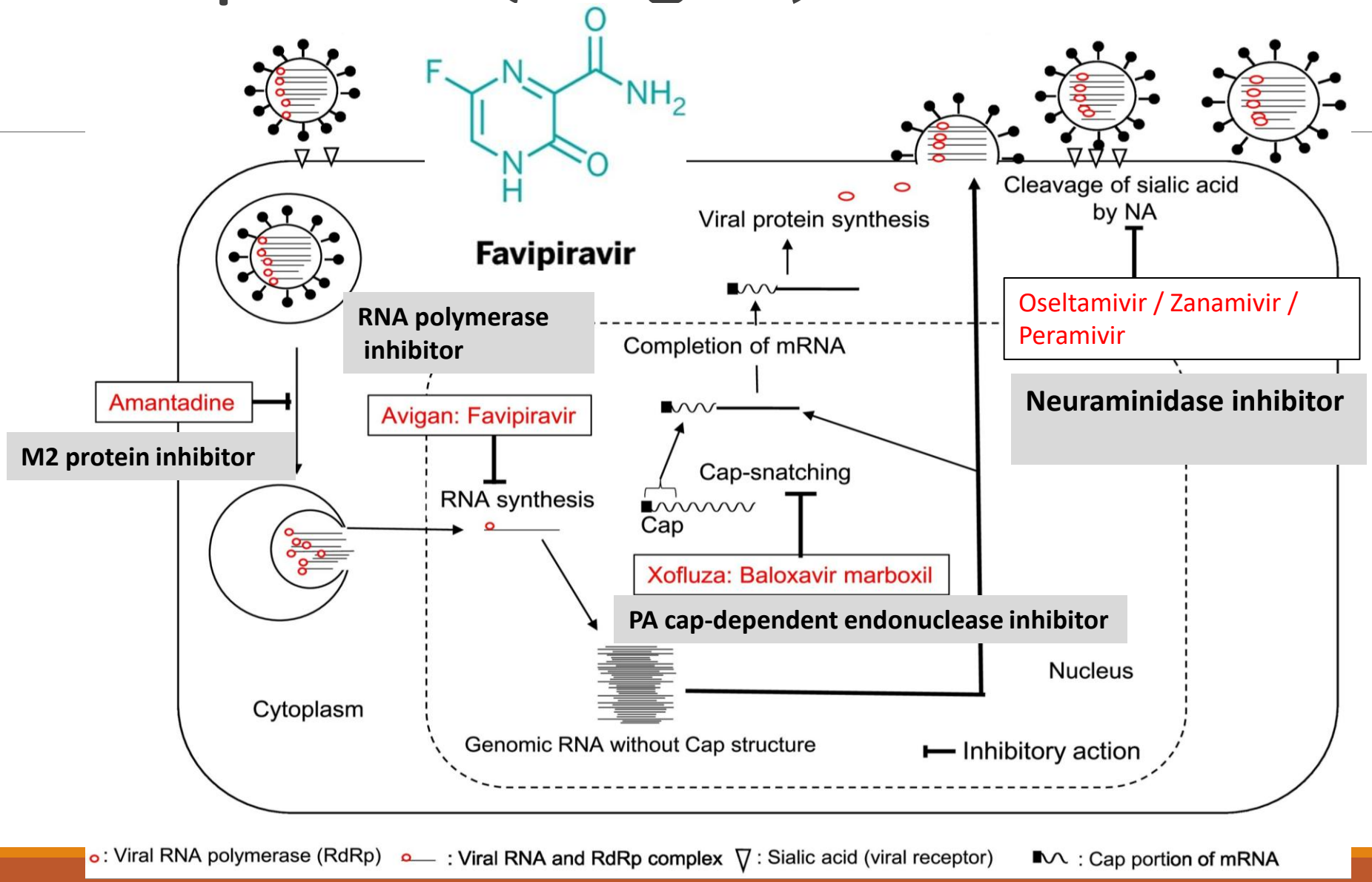
目前抗藥性病毒株並不常見，但仍需持續監測。
如當年流行病毒株為H1N1，需留意NAIs抗藥性。
如當年流行病毒株為H3N2，需留意Baloxavir抗藥性

1	**先確認 ongoing replication**	臨床惡化 ≠ resistance；重症優先 lower respiratory tract sample
2	**看 host 與時間**	免疫抑制、幼兒、prolonged high viral burden → treatment-emergent resistance risk 高
3	**回頭看 drug pressure**	Oseltamivir → NA mutations (H275Y 等)；Baloxavir → PA/I38X
4	**換 non-cross-resistant mechanism**	H275Y 常影響 oseltamivir + peramivir；zanamivir 多數仍保留活性。I38X → 改用NAI

Treatment-emergent resistance 常見 ≠ community resistance 盛行率高。

CDC 2026; Hui DS 2026; resistance modeling and prior trial-derived emergence data.

Favipiravir（Avigan）



Favipiravir 目前建議

- 專案進口藥物但無我國藥物許可證，使用對象為符合疾病管制署公布之新型A型流感通報定義者，經使用oseltamivir及zanamivir等抗流感病毒藥劑治療無效，且經醫師評估及病患/家屬同意使用者
- 第 1 日每回服用 1600mg，每日2回。第 2 至 5 天每回 600mg，每日2回。總投藥期間為 5 天
- 本藥劑具致畸胎性， 兒童、已知/準備懷孕者及授乳者皆不可使用。
- 老人、痛風患者或有痛風病史者、高尿酸血症者、肝功能不良 或腎功能不良者，需慎重投藥。

2026 成人常用抗流感藥：怎麼選？

Route、族群與限制，比背所有副作用更重要

藥物	成人常用療程	常見定位	主要限制 / caveat
Oseltamivir	75 mg BID × 5 d (腎功能調整)	住院 / 高風險；孕婦首選	GI adverse events；H275Y；critical illness evidence now challenged
Zanamivir	10 mg inhaled BID × 5 d	NAI resistance(H275Y) 時可考慮	氣喘/COPD bronchospasm；不適合 ventilated severe illness
Peramivir	IV 300-600mg*1 (腎功能調整)	無法 enteral 時替代	住院重症 clinical benefit 證據不足；H275Y 可 cross-resistance
Baloxavir	**<80 kg 40 mg once ≥80 kg 80 mg once**	**早期 uncomplicated；B 型可偏好, viral decline 更快**	**pregnancy / severe immunosuppression / hospitalized severe data limited；I38X**

2025–2026：更新的 4 件事

1	**門診 patient-important benefit 仍有限**	2025 NMA：症狀約縮短 0.75–1.02 天；死亡與住院效益有限或不確定。
2	**Baloxavir 的 in-vivo antiviral potency 最強**	AD ASTRA：viral RNA clearance +86%，但完整症狀緩解沒有明顯差異。
3	**重症 oseltamivir 出現 RCT 反向訊號**	REMAP-CAP：organ-support ICU mortality 對 oseltamivir 不利；目前仍是 preprint。
4	**抗藥性要分「治療後出現」與「族群盛行」**	台灣 H1N1 曾見較高 NAI resistance；美國 2025–26 整體仍低，Baloxavir 0/4,491。

Gao et al. JAMA Intern Med 2025; Jittamala et al. Lancet Infect Dis 2026; REMAP-CAP 2026 preprint; CDC surveillance.

用藥框架： Take-home messages

低風險門診	**Benefit modest**	Baloxavir / oseltamivir 都可；shared decision
高風險門診	**Treat early**	不要等待 confirmation；Influenza B 可偏 Baloxavir
住院、尚未 organ support	**Treat now**	現行多數 guideline 仍支持 oseltamivir ASAP
ICU + organ support	**Evidence conflict**	REMAP-CAP 不利；澳洲 interim guideline 反對；仍待 peer-reviewed publication / broader guidance
Prolonged shedding / IC host	**Think resistance**	確認 replication → genotype/phenotype if possible → non-cross-resistant mechanism

severity setting 的 evidence 不能互相外推。

Synthesis: CDC 2026; JAMA Intern Med 2025; AD ASTRA 2026; REMAP-CAP 2026 preprint; Taiwan CDC surveillance.





Thank you