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A budget Impact Analysis of Reducing Viral Transmission with Baloxavir Marboxil Treatment for Seasonal Influenza in Japan <u>Naoya Itsumura¹, Shogo Miyazawa², Satoki Fujita²</u>



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OBJECTIVES

- Baloxavir marboxil (baloxavir) is an oral antiviral that rapidly stops influenza viral shedding. However, the impact of reduced viral shedding on the number of infections and the resulting budget impact are unknown.
- This study aimed to investigate the reduction in the total number of infections and the budget impact of baloxavir compared to neuraminidase inhibitors (NAIs) using a SEIR (susceptible, exposed, infected, recovered) model.

RESULTS

- The SEIR model estimated greater reductions in infections with increased baloxavir treatment (Table 2). The baloxavir share for adults was varied in the model based on the share in 2018/2019 season (baloxavir vs NAIs for adults: 50% vs 50%; for children: 20% vs 80%).
- We estimated that influenza patients decreased from 11.7 million to 9.6 million (18.3% reduction) if 10% of NAIs for adults were replaced with baloxavir in the 2018/2019 season.

METHODS

- The population-level SEIR model estimated the attack rates by comparing the impact of treatment ratio of baloxavir and NAIs to linking the time of infectious virus negativity, using the clinical trial data of baloxavir compared to oseltamivir for the influenza treatment.
- The population was stratified into four subgroups: 1) otherwise healthy children, 2) high-risk children, 3) otherwise healthy adolescents and non-elderly adults, and 4) high-risk adolescents, high-risk adults, and the elderly (Figure 1).
- The parameters were calculated using Japanese real-world data from the 2018/2019 season (Figure 1), because there were almost no influenza cases during the COVID-19 pandemic. The budget impact analysis was conducted at the total population level, incorporating the attack rates from the SEIR model.

Constant Flow(change per day)



The budget impact was calculated to be a benefit of 6.0 billion JPY in drug costs, 16.0 billion JPY in medical costs, and 20.7 billion JPY in labor productivity losses (Figure 2).

Baloxavir	Share of antiviral treatment				Proportion of
increase or	Baloxavir for	NAIs for	Baloxavir for	NAIs for	infected
decrease scenario	Adults	Adults	Children	Children	population
-20%	30%	70%			14.1%
-10%	40%	60%			11.9%
Base case	50%	50%	20%	80%	9.9%
+10%	60%	40%			8.0%
+20%	70%	30%			6.5%

Table 2: Proportion of infected population with varying shares of baloxavir or NAIs The base case is the most similar estimation to the 2018/2019 season in Japan.





Figure 1: Structure of the SEIR model

B = Exposed rate, $1/\lambda$ = Infection rate, $1/\gamma$ = recover rate, Tp = Treated patients, t = Tamiflu (oseltamivir) treatment, x = Xofluza (baloxavir) treatment, H = High-risk group, Er = Emerging resistant virus, N/P = No treated patients or Patients infected resistance virus, SEIR = Susceptible, Exposed, Infected, Recovered.

Variable	Inputs	Source			
Population size	10,000	Assumption			
Initial number of infected	10	Assumption			
Susceptible (S)	66.4%	Calculation from RWD in Japan			
Transmittability (β)	0.25	Calculation from RWD in Japan			
Infected but not infectious (λ)	1 day	Miyazawa et al., (2022)			
Antiviral treatment rate	92.1%	Calculation from RWD in Japan			
Adults in the population	47.4%	Calculation from 2018/19 season data			
HR proportion in children	44.8%	Calculation from 2018/19 season data			
HR proportion in adults	44.1%	Dronova et al., (2021)			
Simulation period	365 days	Influenza one season			
Time to cessation of viral shedding (γ)					
No antiviral in OwH	4.71 days	Estimating from CAPSTONE-1 trial*			
Oseltamivir in OwH	3.83 days	Estimating from CAPSTONE-1 trial*			
Baloxavir in OwH	2.11 days	Estimating from CAPSTONE-1 trial*			
No antiviral in HR	4.53 days	Estimating from CAPSTONE-2 trial**			
Oseltamivir in HR	3.90 days	Estimating from CAPSTONE-2 trial**			
Baloxavir in HR	2.72 days	Estimating from CAPSTONE-2 trial**			



Figure 2: Reductions in number of treatment, drug costs, medical costs, and labor productivity losses with increasing baloxavir share

a) We assumed that the market share of drugs other than baloxavir was not changed.

b) Drug costs were calculated based on age and weight indication of each drug.

c) Medical costs were calculated based on GP visit fee and diagnostic tests.

d) Labor productivity losses were calculated by assuming that influenza infection caused two days of absence from work and working adults lose the average wage each day. JPY = Japanese yen

CONCLUSIONS

Table 1: Key Inputs and assumptions for the SEIR model

Due to lack of data, the time to cessation of viral shedding by NAIs (laninamivir, zanamivir, and oseltamivir) was assumed to be equal to oseltamivir. HR = High-risk, OwH = Otherwise health

- Compared to NAIs, baloxavir treatment may result in fewer influenza cases and could save costs of billions of JPY per influenza season from public healthcare payers' perspective and social perspective in Japan.
- As influenza epidemic have reappeared in Japan from the 2023/2024 season, the results of the transmission model and the budget impact analysis need to be updated to reflect the post COVID-19 pandemic reality.

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Conflict of interest: NI, SM, and SF are employees of Shionogi & Co., Ltd.

^{*} Hayden FG, Sugaya N, Hirotsu N, et al. Baloxavir Marboxil for Uncomplicated Influenza in Adults and Adolescents. N Engl J Med. 2018;379(10):913-923.

^{**} Ison MG, Portsmouth S, Yoshida Y, et al. Early treatment with baloxavir marboxil in high-risk adolescent and adult outpatients with uncomplicated influenza (CAPSTONE-2): a randomised, placebo-controlled, phase 3 trial. Lancet Infect Dis. 2020;20(10):1204-1214.