

Pandemic (H1N1) 2009 briefing note 12

25 SEPTEMBER 2009 | GENEVA -- **Growing international experience in the treatment of pandemic H1N1 virus infections underscores the importance of early treatment with the antiviral drugs, oseltamivir or zanamivir. Early treatment is especially important for patients who are at increased risk of developing complications, those who present with severe illness or those with worsening signs and symptoms.[1]**

The experience of clinicians, including those who have treated severe cases of pandemic influenza, and national authorities suggests that prompt administration of these drugs following symptom onset reduces the risk of complications and can also improve clinical outcome in patients with severe disease.

This experience further underscores the need to protect the effectiveness of these drugs by minimizing the occurrence and impact of drug resistance.

High-risk situations for development of drug resistance

WHO encourages clinicians to be alert to two situations that carry a high risk for the emergence of viruses resistant to oseltamivir.

The risk of resistance is considered higher in patients with severely compromised or suppressed immune systems who have prolonged illness, have received oseltamivir treatment (especially for an extended duration), but still have evidence of persistent viral replication.

The risk of resistance is also considered higher in people who receive oseltamivir for so-called "post-exposure prophylaxis" following exposure to another person with influenza, and who then develop illness despite taking oseltamivir.

In both of these clinical situations, health care staff should respond with a high level of suspicion that oseltamivir resistance has developed. Laboratory investigation should be undertaken to determine whether resistant virus is present and appropriate infection control measures should be implemented or re-enforced to prevent spread of the resistant virus.

When a drug-resistant virus is detected, WHO further recommends that an epidemiological investigation be undertaken to determine whether onward transmission of the resistant virus has occurred. In addition, community surveillance for oseltamivir-resistant pandemic H1N1 virus strains should be enhanced.

In general, WHO does not recommend the use of antiviral drugs for prophylactic purposes. For people who have had exposure to an infected person and are at a higher risk of developing severe or complicated illness, an alternative option is close monitoring for symptoms, followed by prompt early antiviral treatment should symptoms develop.

WHO has also recommended against the use of a particular antiviral where the virus is known or highly likely to be resistant to it. For this reason, zanamivir is the treatment of choice for patients who become ill while on oseltamivir prophylaxis.

Oseltamivir-resistant viruses

Systematic surveillance conducted by the Global Influenza Surveillance Network, supported by WHO Collaborating Centres and other laboratories, continues to detect sporadic incidents of H1N1

pandemic viruses that show resistance to oseltamivir. To date, 28 resistant viruses have been detected and characterized worldwide.[2]

All of these viruses show the same H275Y mutation that confers resistance to the antiviral oseltamivir, but not to the antiviral zanamivir. Zanamivir remains a treatment option in symptomatic patients with severe or deteriorating illness due to oseltamivir-resistant virus.

Twelve of these drug-resistant viruses were associated with the use of oseltamivir for post-exposure prophylaxis. Six were associated with the use of oseltamivir treatment in patients with severe immunosuppression. Four were isolated from samples from patients receiving oseltamivir treatment.

A further two were isolated from patients who were not taking oseltamivir for either treatment or prophylaxis. Characterization of the remaining viruses is under way.

These numbers are comparatively small at present. Worldwide, more than 10,000 clinical specimens (samples and isolates) of the pandemic H1N1 virus have been tested and found to be sensitive to oseltamivir.

Current conclusions

These data support several conclusions. Cases of oseltamivir-resistant viruses continue to be sporadic and infrequent, with no evidence that oseltamivir-resistant pandemic H1N1 viruses are circulating within communities or worldwide.

To date, person-to-person transmission of these oseltamivir resistant viruses has not been conclusively demonstrated. In some situations, however, local transmission may have occurred, but without any further onward or ongoing transmission.

Except for immunocompromised patients, those infected with an oseltamivir-resistant pandemic H1N1 virus have experienced typical uncomplicated influenza symptoms. No evidence suggests that oseltamivir-resistant viruses are causing a different or more severe form of illness.

The occurrence of oseltamivir-resistant viruses is expected and is consistent with observations from early clinical trials. As use of antiviral drugs continues to grow, further reports of drug-resistance viruses are certain to occur. WHO and its network of collaborating laboratories are closely monitoring the situation and will issue information and advice on a regular basis as indicated.

[1] [Briefing Note on recommendations for use of antivirals](#)

[2] [Weekly updates on cases of oseltamivir resistant pandemic H1N1 virus](#)

Source:

http://www.who.int/csr/disease/swineflu/notes/h1n1_antiviral_use_20090925/en/index.htm
