Influenza A Appears Resistant to Oseltamivir

BY SHERRY BOSCHERT

The dominant strain of influenza A during the current flu season is nearly completely resistant to oseltamivir because of a mutation that leaves its virulence intact, according to two studies that upset long-held ideas about oseltamivir-resistant influenza A (H1N1) viruses.

Findings from a third study bolster the rationale for widespread vaccination.

Taken together, the findings from these three studies should motivate more people to get annual influenza vaccinations, especially health care workers, since treatment options are now more limited, said Dr. Gregory A. Poland, who was not a participant in the studies. He is the American College of Physicians liaison to the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices (ACIP).

In the first study, Dr. Nila J. Dharan of the CDC's influenza division in Atlanta, and associates, tested 268 influenza A (H1N1) isolates from the 2008-2009 season and found that 99% were oseltamivir (Tamiflu) resistant (JAMA 2009 [doi:10.1001/jama.2009.294]).

Such findings shore up concerns raised by a December 2008 CDC health advisory that reported resistance to oseltamivir in 98% of 50 influenza A (H1N1) viruses from 12 states in the early part of the 2008-2009 influenza season. As recently as the 2006-2007 influenza season, oseltamivir-resistant influenza was very uncommon. In the 2007-2008 season, however, influenza A (H1N1) comprised 19% of circulating influenza viruses, and 12% of 1,155 H1N1 viruses tested from 45 states showed oseltamivir resistance, according to Dr. Dharan and associates. About 55% of influenza types isolated so far by the CDC in the 2008-2009 season are oseltamivir-resistant H1N1.

Previously it was thought the mutation conferring oseltamivir resistance weakens the virus' ability to be transmitted from person to person and to sicken or kill, but Dr. Dharan's study and another by Dr. Jairo Gooskens dispel those notions. In Dr. Dharan's study, 3% of 142 patients whose resistant viruses were tested by the CDC died of influenza.

Dr. Gooskens of Leiden (the Netherlands) University, and associates performed gene sequencing analysis on viruses from four patients in a nosocomial outbreak of oseltamivir-resistant influenza A (H1N1) at one hospital. The virus spread from the index patient to three others, two of whom died, and possibly to five health care workers (JAMA 2009 [doi:10.1001/jama.2009.297]).

In neither study did use or overuse of oseltamivir appear to contribute to viral resistance, a fact that "frankly, has caught us with our intellectual pants down. That really did surprise us," said Dr. William Schaffner, chair of preventive medicine at Vanderbilt University, Nashville, Tenn., and the Infectious Diseases Society of America liaison to the ACIP. He did not participate in the studies.

At an ACIP meeting held in late February, committee members "acknowledged that we are still a little flummoxed about how it is that these viruses could have spread not only within the United States but globally so rapidly," he said.

The third study analyzed more than a million active-duty members of the U.S. military during three influenza seasons. The trivalent inactivated vaccine (TIV) was more effective than was the live attenuated influenza vaccine (LAIV) or no vaccine in protecting this annually immunized cohort, reported Zhong Wang, Ph.D., of the Armed Forces Health Surveillance Center, Silver Spring, Md., and associates (JAMA 2009;301:945-53).

The study investigators all reported having no conflicts of interest related to the studies. Dr. Schaffner has been a consultant for, or received funding from, GlaxoSmithKline, Novartis, Sanofi Pasteur, and MedImmune, which make influenza vaccines or treatments. Dr. Poland has been a consultant for, or received funding from, Dynavax, Novavax, Merck & Co., GlaxoSmithKline, Novartis Vaccines, CSL Biotherapies, PowderMed, Avianax, and Protein Sciences. ■

Updates on CDC influenza antiviral recommendations can be monitored at www.cdc.gov/flu/professionals/antivirals.