High-Dose Flu Vaccine Prevents Symptomatic Influenza and Reduces Hospitalizations

Fluzone High-Dose, manufactured by Sanofi Pasteur, is an influenza vaccine designed specifically for adults 65 years or older to improve antibody responses, as well as to protect them against influenza subtype viruses contained in the vaccine.[1] In a presentation at the 6th Annual Live Meeting of the ACO & Emerging Healthcare Delivery Coalition™, hosted by T*he American Journal of Managed Care*® on October 20-21, 2016, Ayman Chit, PhD, presented results from multiple clinical trials demonstrating the efficacy of the Fluzone High-Dose vaccine.

Dr Chit, senior director for Health Economics and Outcome Research at Sanofi Pasteur, explained that individuals 65 years or older experience the greatest burden of influenza, accounting for 90% of total influenza-related deaths and 37% of influenza-associated hospitalizations in the United States.[2-4] Influenza can aggravate existing chronic illnesses and increase the risk of hospitalization for serious respiratory and cardiovascular conditions.

Vaccines that protect against influenza are available; however, their effectiveness is substantially compromised in the population of adults 65 or older, with responses in 26% to 52% of vaccinated individuals compared with much higher (62% to 76%) vaccine effectiveness among those aged 15 to 64 years.[5]

As a natural process of aging, immunosenescence is associated with decreased immunologic response to vaccines and lower vaccine effectiveness in the older population. Age-related impairments in antibody response may leave older adults more vulnerable to influenza and its associated complications.

Fluzone High-Dose was developed to address the need for a vaccine specifically intended for the population of adults 65 years or older. The high-dose formulation contains 4 times the amount of hemagglutinin (HA) in a Fluzone standard-dose vaccine, which allows for the induction of a superior immunogenic response of antibodies to HA and neutralization of influenza virus infectivity. Higher postvaccination antibody titers to H1N1 and H3N2 influenza and B virus are associated with influenza protection.[1]

Dr Chit presented results from an efficacy trial published by DiazGranados et al.[6] In the trial, 32,000 elderly adults were randomized 1:1 for vaccination with Fluzone High-Dose or Fluzone standard dose at the beginning of 2 influenza seasons (2011-2012 and 2012-2013). Immunization with Fluzone High-Dose resulted in a 24.2% reduction in symptomatic influenza caused by any influenza viral type or subtype. Vaccination with Fluzone High-Dose also reduced the incidence of influenza-associated illnesses

and hospitalizations throughout the trial. Key results:

- 51% reduction of culture-confirmed flu caused by viral subtypes, antigenically similar strains to those contained in the annual vaccine formulation.
- 40% reduction of serious pneumonia.
- 18% reduction of serious cardiorespiratory events.
- 31% reduction in 30-day hospitalizations.

Over the same 2 influenza seasons, Nace et al[7] conducted a randomized controlled trial among 187 senior residents of long-term care facilities. Vaccination with Fluzone High-Dose induced superior antibody responses to influenza type A strains H1N1, H3N2, and B strains compared with standard-dose Fluzone vaccine. As a marker of enhanced and durable immune response, antibody titers remained higher 180 days post vaccination. Also, rates of seroconversion—or development of antibodies against influenza virus—were higher 30 days post vaccination in both influenza seasons.

Importantly, because influenza increases hospitalization risk in this population, Chit presented evidence from a cluster-randomized pilot study by Gravenstein et al.[8] The results showed that Fluzone High-Dose significantly reduced hospitalization rates among elderly residents in US nursing homes compared with those receiving standard-dose Fluzone. Elderly residents vaccinated with Fluzone High-Dose had hospitalization reductions of:

- 30% during H3N2-dominated seasons ($P = .006$).
- 7% during H1N1-dominated seasons ($P = .0195$).

Dr Chit presented results from a retrospective study by Izurieta et al.[9] In this study, Medicare claims were used to identify a well-balanced cohort of approximately 2.5 million beneficiaries 65 years or older who had been vaccinated during the 2012 to 2013 influenza season. The results of this study demonstrated that, compared with standard-dose influenza vaccines, vaccination with Fluzone High-Dose induced:

- 22% greater protection against probable influenza illness.
- 22% better protection against influenza-related hospitalizations and emergency department visits.

The clinical efficacy of Fluzone High-Dose is supported by data from numerous clinical trials, which indicate that vaccination enhances protection against influenza through stimulation of greater immune response compared with Fluzone standard dose within the population of individuals 65 years or older.

REFERENCES

1. Fluzone High-Dose vaccine [prescribing information]. Swiftwater, PA: Sanofi Pasteur Inc; 2015.
2. Fiore AE, Shay DK, Broder K, et al; CDC. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. *MMWR Recomm Rep*. 2009;58(RR-8):1-52.
3. Poland GA, Mulligan MJ. The imperative of influenza vaccines for elderly individuals—an evolving story. *J Infect Dis*. 2009;200(2):161-163. doi: 10.1086/599791.
4. Thompson WW, Shay DK, Weintraub E, et al. Influenza-associated hospitalizations in the United States. *JAMA*. 2004;292(11):1333-1340.
5. Monto AS, Ansaldi F, Aspinall R, et al. Influenza control in the 21st century: optimizing protection of older adults. *Vaccine*. 2009;27(37):5043-5053. doi: 10.1016/j.vaccine.2009.06.032.
6. DiazGranados CA, Dunning AJ, Robertson CA, Talbot HK, Landolfi V, Greenberg DP. Efficacy and immunogenicity of high-dose influenza vaccine in older adults by age, comorbidities, and frailty. *Vaccine*. 2015;33(36):4565-4571. doi: 10.1016/j.vaccine.2015.07.003.
7. Nace DA, Lin CJ, Ross TM, Saracco S, Churilla RM, Zimmerman RK. Randomized, controlled trial of high-dose influenza vaccine among frail residents of long-term care facilities. *J Infect Dis*. 2015; 211(12) 1915-1924. doi:10.1093/infdis/jiu622.
8. Gravenstein S, Taljaard M, Gozalo P, et al. Relative effect of high-dose influenza vaccination on hospitalizations of older adults in U.S. nursing homes: results from a cluster-randomized controlled trial [abstract LB-8]. Presented at: IDWeek; October 7-11, 2015; San Diego, CA. https://idsa.confex.com/idsa/2015/webprogram/Paper54095.html. Accessed November 2016.
9. Izurieta HS, Thadani N, Shay DK, et al. Comparative effectiveness of high-dose versus standard-dose influenza vaccines in US residents aged 65 years and older from 2012 to 2013 using Medicare data: a retrospective cohort analysis [erratum in *Lancet Infect Dis*. 2015;15(4):373].. *Lancet Infect Dis*. 2015;15(3):293-300. doi: 10.1016/S1473-3099(14)71087-4.