PUBLICATION CARD

Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults

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INTRODUCTION

- Adults aged ≥65 years are particularly vulnerable to complications associated with influenza and account for most influenza–related hospitalizations and deaths
- The high-dose trivalent, inactivated influenza vaccine (IIV3-HD), containing four times amount of hemagglutinin (HA), is designed to improve the clinical protection for this population

OBJECTIVE

To evaluate the efficacy of IIV3-HD as compared with standard dose trivalent inactivated vaccine (IIV3-SD) against laboratory-confirmed influenza in adults aged ≥65 years.

STUDY CONDUCT

DESIGN	VACCINES	PARTICIPANTS	SEASONS - COUNTRIES
Phase IIIb–IV, multicenter, randomized (1:1), controlled trial	**IIV3-HD** versus **IIV3-SD**	**31,989 participants 65 years of age or older**	**126 centers in the United States and Canada** from 2011-12 to 2012-13

ASSESSMENT

EFFICACY

- Primary endpoint: Laboratory-confirmed influenza at least 14 days after vaccination, caused by any strain, in association with a protocol-defined ILI
  - Superiority criteria: the lower bound of the 95% confidence interval (CI) for relative vaccine efficacy must exceed 9.1%
- Several secondary efficacy and observational effectiveness endpoints were also evaluated, according to various clinical illness definitions, methods of laboratory confirmation, and levels of similarity to the vaccine

SAFETY

- The safety of IIV3-HD had been previously evaluated in a Phase III study; this study focused on serious adverse events (SAEs)

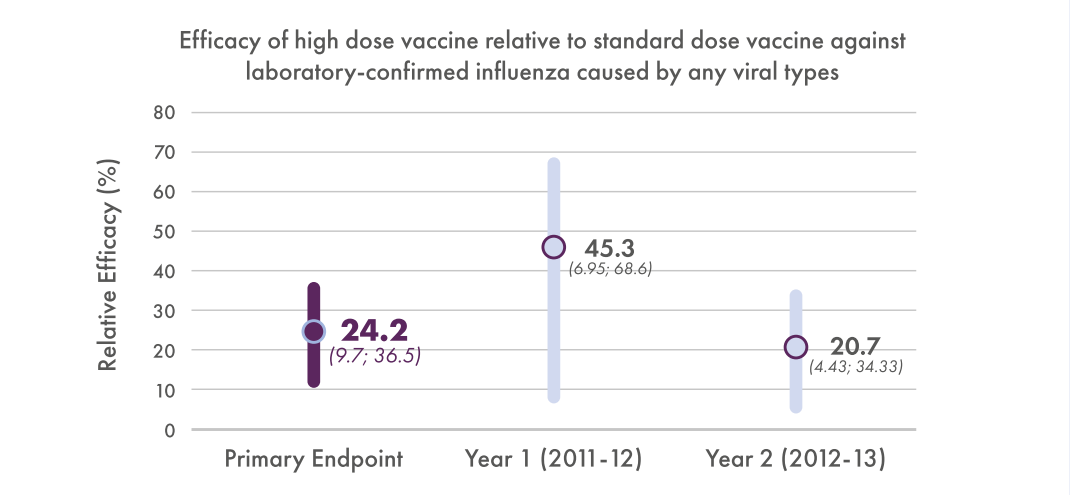
IMMUNOGENICITY (subset participants)

- HAI titer was assayed after 28 days of vaccination
- Geometric mean titers (GMTs) and seroprotection rates (the percentage of participants with an HAI titer ≥1:40) were assessed after 28 days of vaccination

RESULTS

EFFICACY

- The efficacy of IIV3-HD relative to IIV3-SD (primary endpoint) was **24.2%** with a lower bound of the 95% CI of **9.7%**, satisfying the prespecified superiority criterion
- In addition, the point estimate for rVE was consistently positive across influenza types, clinical illness definitions, methods of laboratory confirmation, and study years, even in year 2, where there was a vaccine mismatch



- IIV3-HD was associated with lower rates of several serious events, compared with IIV3-SD group, including pneumonia (risk reduction: 39.8% [95% CI 19.3; 55.1]), cardiorespiratory conditions (risk reduction: 17.7% [95% CI 6.6; 27.4]), and all-cause hospitalizations (risk reduction: 6.9% [95% CI 0.5; 12.8])

SAFETY

- 8.3% participants in the IIV3-HD group and 9% participants in the IIV3-SD group had ≥1 serious adverse event with a relative risk of 0.92 (95% CI, 0.85-0.99) for IIV3-HD
- Three serious adverse events were related to the vaccination, but all were resolved before study completion and none resulted in study discontinuation

IMMUNOGENICITY

- HI antibody GMTs and seroprotection rates after 28 days of vaccination were significantly higher with IIV3-HD than IIV3-SD for all three vaccine strains

STUDY LIMITATIONS

Some of the efficacy estimates according to influenza type, definitions of secondary illness, and confirmation methods were based on a limited number of cases and may therefore lack sufficient precision.

KEY MESSAGES

1. This efficacy RCT showed that IIV3-HD provided improved protection versus IIV3-SD against laboratory-confirmed influenza among adults aged 65 years of age.

2. The overall efficacy of 24.2% against the primary end point indicates that about one quarter of all breakthrough influenza illnesses could be prevented if IIV3-HD were used instead of IIV3-SD.

Access the article

Reference: DiazGranados CA et al. Efficacy of High-Dose versus Standard-Dose Influenza Vaccine in Older Adults; N Engl J Med. 2014; 371: 635-645.
Glossary: **FDA:** Food and Drug Administration; **GMT:** Geometric mean titre; **HA:** hemagglutinin antigen; **HI:** hemagglutination-inhibition; **HD:** high dose; **IIV3-SD:** standard dose trivalent inactivated influenza vaccine; **ILI:** influenza-like illness; **SAE:** serious adverse events.
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