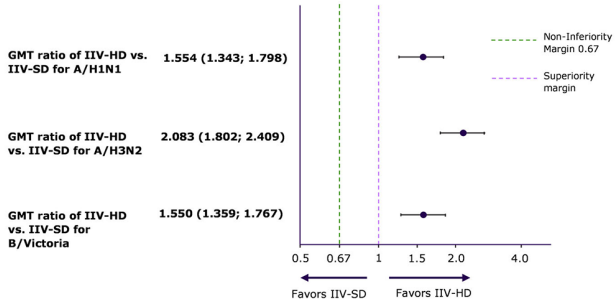
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409. A Phase 3, Randomized, Modified Double-blind Study Demonstrates Immunological Superiority of High-Dose (HD) Over Standard-Dose (SD) Inactivated Influenza Vaccine (IIV) in Adults 50 Through 64 Years of Age

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Background. Adults 50-64 years have reduced immune response to SD influenza vaccines and higher morbidity associated with severe influenza than younger adults. IIV-HD (Fluzone® HD) contains 4 times the antigen as IIV-SD, is preferentially recommended in the US for persons ≥65 years, and has a well-established safety profile. This study aimed to establish noninferiority (NI) and superiority of IIV- HD immune response compared to IIV-SD and assess safety in adults 50-64 years of age.



Abbreviations: CI=Confidence interval; D=Day on study; GMT=Geometric mean titer; IIV-HD=Inactivated influenza vaccine high-dose, IIV-SD=Inactivated influenza vaccine standard-dose

Figure 1. Forest plot - Post-vaccination GMT ratio and 95% CI of IIV-HD compared to IIV-SD at D29

Table 1: Disposition by randomized group

Timepoint		IIV-HD (n [%])	IIV-SD (n [%])	All (n [%])
	Planned	589	589	1178
V01 (D01)	Randomized	590 (100)	590 (100)	1180 (100)
	Present at visit	590 (100)	590 (100)	1180 (100)
	BL performed	585 (99.2)	586 (99.3)	1171 (99.2)
	Injected	585 (99.2)	586 (99.3)	1171 (99.2)
V02 (D29)	Present at visit	568 (96.3)	570 (96.6)	1138 (96.4)
	BL performed	567 (96.1)	570 (96.6)	1137 (96.4)
	Completed the study intervention phase	568 (96.3)	570 (96.6)	1138 (96.4)

Abbreviations: V01=Visit 1; V02=Visit 02; D=Day on study; IIV-HD=Inactivated influenza vaccine high-dose, IIV-SD=Inactivated influenza vaccine standard-dose, BL=Blood sampling

Methods. A Phase 3, randomized, modified double-blind, active-controlled multicenter study (NCT06641180) was conducted in the US (Nov 2024 -Jun 2025). Participants 50-64 years old were randomized 1:1 to either IIV-HD or IIV-SD (Fluarix®, GSK) on Day (D) 01, followed for immunogenicity up to D29 and safety through 6 months. Primary objective was to evaluate NI of IIV-HD by ratio of geometric mean titer (GMT) and seroconversion rate (SCR), measured by hemagglutination inhibition assay (HAI), 28 days postvaccination. If NI was achieved for all 3 strains, IIV-HD superiority was assessed based on GMTs. If achieved, then superiority to a stringent threshold for at least one strain was tested.

Table 2:

A. Non-inferiority and superiority in GMTs of anti-hemagglutinin antibodies for IIV-HD compared to IIV-SD at D29

	IIV-HD		IIV-SD		IIV-HD/IIV-SD					
Antigen/ strain	GMT	(95% CI)	GMT	(95% CI)	GMT ratio	(95% CI)	Non-Inferiority*	Superiority Margin=1#	(98.3 % CI)	Superiority Margin=1.5+
A/H1N1	391	(351; 436)	261	(235; 290)	1.554	(1.343; 1.798)	Yes	Yes	(1.301; 1.856)	No
A/H3N2	661	(592; 738)	328	(291; 370)	2.083	(1.802; 2.409)	Yes	Yes	(1.746; 2.486)	Yes
B/Victoria	946	(859; 1041)	619	(562; 682)	1.550	(1.359; 1.767)	Yes	Yes	(1.321; 1.818)	No

Abbreviations: CI=Confidence interval, GMT=Geometric Mean Titer, IIV-HD=Inactivated influenza vaccine high-dose, IIV-SD=Inactivated influenza vaccine standard-dose, NI=Non-inferiority
*Noninferiority (NI) in GMTs will be demonstrated if the lower limit of the 2-sided 95% CIs of GMT ratio for IIV-HD/IIV-SD is >0.667 for all 3 vaccine matched strains
#Superiority in GMTs will be demonstrated if the lower limit of the 2-sided 95% CIs of GMT ratio for IIV-HD/IIV-SD is >1 for all 3 strains
+Superiority to the stringent threshold will be demonstrated if the lower limit of the 2-sided 98.3% CI for the ratios of GMTs is >1.5 for at least one strain.

B. Non-inferiority in seroconversion rates of anti-hemagglutinin for IIV-HD compared to IIV-SD using at D29

	IIV-HD		IIV-SD		Seroconversion Difference IIV-HD minus IIV-SD		
Antigen/ strain	%	(95% CI)	%	(95% CI)	Difference	(95% CI)	Non-Inferiority*
A/H1N1	74.5	(70.6; 78.0)	56.0	(51.8; 60.2)	18.46	(12.90; 23.86)	Yes
A/H3N2	82.1	(78.6; 85.2)	64.8	(60.6; 68.7)	17.31	(12.16; 22.33)	Yes
B/Victoria	77.0	(73.3; 80.4)	64.8	(60.6; 68.7)	12.23	(6.90; 17.47)	Yes

Abbreviations: CI=Confidence interval, IIV-HD=Inactivated influenza vaccine high-dose, IIV-SD=Inactivated influenza vaccine standard-dose, NI=Non-inferiority
*NI in seroconversion will be demonstrated if the lower limit of the 2 sided 95% CI is >-10% for all 3 strains.

Results. 1171 participants were vaccinated; 1137 (96.4%) provided a blood sample at D01 and D29 (Table 1). Median age was 57 years; majority were female 54.9% and of white race 61.4%. Previous season influenza vaccination in 31.9% (IIV-HD) vs 33.4% (IIV-SD).

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IIV-HD induced higher HAI GMTs and SCR than IIV-SD (Fig 1, Table 2). Coprimary immunogenicity endpoints of NI for HAI GMTs and SCR were achieved for all 3 vaccine matched strains.

IIV-HD also demonstrated a superior immune response vs IIV-SD by D29 GMT ratio (95% confidence interval [CI] lower limit >1) for all 3 strains. In addition, stringent threshold superiority was achieved for H3N2 for GMT ratio (98.3% CI lower limit >1.5).

The expected safety profile was confirmed in this age group through D29.

Conclusion. In adults 50–64-years of age, IIV-HD demonstrated robust and superior immune responses to IIV-SD for all 3 influenza strains. IIV-HD met stringent superiority criteria for the H3N2 strain indicating HD H3N2 antibody levels are at least 50% higher than SD. These results support the safe and potential use of IIV-HD in this age group.

Disclosures. All Authors: No reported disclosures

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