

# Pilot Study Evaluating the Safety and Efficacy of Dose Sparing Intradermal Administration of Influenza Vaccine in HIV-Positive Patients

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## Abstract

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### Background:

The United States has experienced a shortage of inactivated influenza vaccine during the last three influenza seasons, leaving many patients (pts) at risk. The capability of extending existing vaccine supplies by using alternative routes of vaccination [e.g., intradermal (ID)], requiring smaller doses, as a means of "stretching" available doses of influenza vaccine, could have important public health implications. This would potentially enable, despite the current limited supply of the vaccine, vaccination of many more pts than would otherwise be possible.

### Methods:

We compared antibody response to reduced ID dosing of the influenza vaccine, to standard intramuscular (IM) dosing, in HIV positive pts. The objective of this study was the comparison of the immunogenicity and safety of the candidate vaccine administered intradermally at a reduced dose (0.1 mL) compared with the reference influenza vaccine administered IM at the standard dose (0.5 mL). The patients were randomized on 2:1 basis to:

- Arm A: receiving 0.1 mL of influenza vaccine via ID injection,
- Arm B: receiving 0.5 mL of influenza vaccine via IM injection.

Serological titers [influenza A and B] were obtained at baseline and at week-4.

### Results:

Fifty-three pts were enrolled in the ID-arm [follow-up titers available on 43]. Thirty-five pts were enrolled in the IM-arm [follow-up titers available on 26]. Both injections were well tolerated. The major side effect of ID-injection was erythema at the site, which resolved within 2-3 days. The baseline mean CD4-count and HIV-RNA log<sub>10</sub> were 467 cells/mm<sup>3</sup> [110-1414], 2.35 log<sub>10</sub> copies/mL [1.69-5.6] in ID-arm, and 464 cells/mm<sup>3</sup> [100-1728], 2.5 log<sub>10</sub> [1.69-5] in IM-arm respectively. The percentage of responders [>1 fold change in the titer] was 42% (18/43 pts) in ID-arm vs. 35% (9/26 pts) in IM-arm.

### Conclusion:

The reduced dose intradermal injection of influenza vaccine is safe and appears equally, if not more immunogenic, than standard intramuscular injection. This approach has major public health implication and further investigation is urgently warranted.

## Results

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## Introduction

- The United States has experienced a shortage of inactivated influenza vaccine during the last three influenza seasons, leaving many patients (pts) at risk.
- The capability of extending existing vaccine supplies by using alternative routes of vaccination [e.g., intradermal (ID)], requiring smaller doses, as a means of "stretching" available doses of influenza vaccine, could have important public health implications.
- This would potentially enable, despite the current limited supply of the vaccine, vaccination of many more pts than would otherwise be possible.

## Methods

- We compared antibody response to reduced ID dosing of the influenza vaccine, to standard intramuscular (IM) dosing, in HIV positive pts.
- The objective of this study was the comparison of the immunogenicity and safety of the candidate vaccine administered intradermally at a reduced dose (0.1 mL) compared with the reference influenza vaccine administered IM at the standard dose (0.5 mL). The patients were randomized on 2:1 basis to:
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## Discussion

- The dermis contains dendritic cells, the most potent antigen-presenting cells.
- Dendritic cells induce cell-mediated immune responses (CD4+ and CD8+ T-cell responses) and will enhance antibody production by B-cells.
- This route of administration not only requires less "quantity of vaccine" but also will result in better immune response from the host.

## Conclusions

- The reduced dose intradermal injection of influenza vaccine is safe and appears equally, if not more immunogenic, than standard intramuscular injection.
- This approach should be evaluated for other vaccinations, as it may improve the antibody responses and the rate of seroconversion.
- This approach also has major public health implication, particularly in the event of a pandemic, and its further investigation is urgently warranted.