Intradermal influenza vaccination

Clinical data and first experience from its use in a routine vaccination programme

Clemens Vlasich, MD, MSc
Agenda

• New Micro-Injection System for intradermal vaccination

• IDflu® - Clinical data
  – Immunogenicity
  – Safety

• First experiences in Australia and in Argentina
Intradermal vaccine administration

- **Skin, the first line of defence**
  - Because it interfaces with the environment, the skin plays a major part in protecting against pathogens.

- **Dermis offers direct access to the immune system, just under the skin surface**
  - Beneath the thin epidermis, the dermis is a tough, flexible and very elastic layer between 1.5 and 3 mm thick.

- **Dermal layer, a highly immunocompetent organ**
  - Thanks to its:
    - High concentration in dendritic cells
      - These cells can control the magnitude, quality and memory of the ensuing immune response.
    - Major vascular networks
      - The density of both lymphatic vessels and blood capillaries favours rapid cellular and antigen exchange for direct access to lymph nodes.

---

4. Bannister LH. In: Gray’s Anatomy 1999
Healthcare Provider explanations for why adults may not receive influenza vaccine

<table>
<thead>
<tr>
<th>Explanation</th>
<th>Physicians (n = 100)</th>
<th>PA/NP/RN (n = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient does not make regular well visits</td>
<td>83%</td>
<td>73%</td>
</tr>
<tr>
<td>Concern about side effects, that it will cause illness</td>
<td>87</td>
<td>87</td>
</tr>
<tr>
<td>Lack of knowledge about illness prevention</td>
<td>62%</td>
<td>75%</td>
</tr>
<tr>
<td>No effective reminder system</td>
<td>62%</td>
<td>63%</td>
</tr>
<tr>
<td>Fear of needles</td>
<td>71%</td>
<td>68%</td>
</tr>
<tr>
<td>Inadequate insurance coverage</td>
<td>61%</td>
<td>67%</td>
</tr>
<tr>
<td>Not going to same physician regularly</td>
<td>59%</td>
<td>65%</td>
</tr>
<tr>
<td>Unaware of vaccination schedule</td>
<td>50%</td>
<td>56%</td>
</tr>
<tr>
<td>Confused about recommended vaccination schedule</td>
<td>50%</td>
<td>45%</td>
</tr>
<tr>
<td>Think healthy people don’t need it</td>
<td>66%</td>
<td>63%</td>
</tr>
</tbody>
</table>

PA=physician assistant; NP=nurse practitioner; RN=registered nurse; 1

Between 10% (GPs; n = 520) to 55% (Pharm.; n = 243) of patients would be discouraged to get vaccinated because of their fear of the needle 2

A new approach to intradermal vaccination

The Micro-Injection System
The Micro-Injection System – Technical description

- Pre-filled glass syringe (0.1 ml)
- Microneedle specifically designed for perpendicular insertion into skin
- Depth of insertion
  1.5 mm from the skin’s surface
- Microneedle smaller and thinner than needle used for IM vaccination
  - Length – 1.5 mm vs. 16 mm
  - Nominal Outer Diameter
    30 G (0.31 mm) vs. 25 G (0.51 mm)

Easy access to intradermal vaccination with an innovative MIS

Perpendicular injection

Use index finger to push on plunger

After injection, push firmly with the thumb to activate the needle shielding system

- No needle stick injuries
- No illicit re-use
IDflu®: Short and thin needle ensuring a minimally invasive injection, reassuring for patients

Needle length & diameter defined according to skin thickness evaluation

IDflu® – Combined technological advances

Micro-Injection System
safely delivers exactly the right volume of vaccine to the dermis

Influenza vaccine formulation and production

Concentrated formulation

Laurent A et al. Vaccine 2007; 25: 6423-6430
IDflu®: Seasonal influenza vaccination for adult and elderly populations

- Split inactivated flu virus vaccine – three strains
  - A/H1N1/California/07/2009
  - A/H3N2/Perth/16/2009
  - B/Brisbane/60/2008
- No adjuvant
- Indications
  - 9μg: 18-59 years of age
  - 15μg: ≥60 years
- 26 February 2009
  Marketing authorisation granted by the European Commission
Clinical Data
# Core clinical trial summary

## Adults
**18-59 years**
9 µg HA/strain

- **Phase II**
  - Dose ranging 3, 6 and 9 µg ID
  - Immunogenicity + safety 9 µg ID vs 15 µg IM

**Elderly**
**≥60 years**
15 µg HA/strain

- **Phase II**
  - Dose ranging 15 or 21 µg ID vs 15 µg IM

- **Phase III**
  - Lot consistency Immunogenicity + safety
  - Superiority testing 15 µg ID vs 15 µg IM

In all the studies, the control vaccine was VAXIGRIP® (15 µg HA/strain)

---

Sanofi Pasteur - Internal data
IDflu® 9 µg

Phase III study in adults (18-59 y)

Immune responses

• IDflu® 9 µg as immunogenic as a reference 15 µg IM vaccine

• Three EMEA criteria met for all three strains

Arnou R. et al. Human Vaccine 2010;6(4)1-9
ClinicalTrials.gov # NCT 00383539
Antibody persistence
IDflu® 9 µg, Phase II study in adults (18-58 y.)

Leroux-Roels I et al, Vaccine 2008; 26: 6614-9
ClinicalTrials.gov #NCT00258934
**IDflu® 15 μg**  
**Phase III study in elderly (≥60y.)**  
**Immune responses**

Immune responses significantly higher with ID vaccine for all strains and criteria

*Significantly higher vs IM vaccine, p<0.05

Arnou et al. Vaccine 2009;27:7304-12  
ClinicalTrials.gov #NCT00383526
IDflu® 15 µg
vs. MF59 adjuvanted influenza vaccine

• Open-label, multicentre, randomised study in volunteers ≥65 years
  – IDflu® 15µg
  – Subunit MF59 adjuvanted vaccine

➢ Study conclusions

Immunogenicity and safety of the intradermal vaccine are comparable to an adjuvanted vaccine in elderly persons

Van Damme et al, BMC Infectious Diseases 2010, 10:1340
Systemic reactogenicity

% with solicited reactions within 7 days of vaccination

- Adults 18-59 years
  - 9 µg ID

- Elderly ≥60 years
  - 15 µg ID

Comparable systemic safety profile

- Mainly mild reactions, started within 3 days of vaccination, lasted 3 days or less

Pooled analysis. Sanofi Pasteur Internal Data
Safety findings according to EMA safety criteria

IDflu® and conventional flu vaccine (IM) have similar, favourable safety profiles based on EMA criteria.
Pooled analysis in adults (<60 years). N: ID=2384, IM=842. ID vaccine formulated at 9 µg HA/strain.

7-day reaction profile
Intanza® 9µg, in adults 18-59 y.

% individuals with reactions from Day 0 to Day 7

Erythema

ID

IM

Injection site pain

ID

IM

<2.5 cm

≥2.5 to <5 cm

≥5 cm

Mild

Easily tolerated

Moderate

Interferes with daily activities

Severe

Incapacitating

NCT00258934
NCT00383539
**Vaccinees Perception of Injection (VaPI) questionnaire**

Local reactions have little impact on vaccinees’ activities of daily living

- 97% in the 15 µg group and 96% in the 9 µg group considered local reactions ‘totally acceptable’ or ‘very acceptable’
- 90% of above 60 year old and more than 80% of 18-59 year old adults vaccinated with IDflu® would probably or definitely want to be vaccinated again the following year

Intradermal influenza vaccination
First experiences in the Southern hemisphere

• Launch
  – in Australia and New Zealand in April 2010
  – In Argentina in July 2010

• Southern hemisphere 2010 formulation
  • A/H1N1/California/07/2009
  • A/H3N2/Perth/16/2009
  • B/Brisbane/60/2008
Australia – Patient acceptability study

- Healthy adults
- Influenza vaccination at an Occupational Health or General Practice Clinic in May 2010
- Patients had the choice – ID 9µg or IM 15µg
- Questionnaire for ID vaccinees after injection (n=1.402)
- Descriptive analysis
Australia – Patient acceptability study

Satisfaction with intradermal vaccine received

- Very satisfied: 78%
- Satisfied: 19%
- Somewhat satisfied: 2%
- Not satisfied: 0%
- Don't know: 0%
- Not answered: 1%

Base: all subjects

Patient Acceptability study. Sanofi Pasteur, data on file.
Australia – Patient acceptability study

Reasons for satisfaction with intradermal vaccine

- The injection was minimally painful: 51%
- The administration process was quick: 36%
- I was reassured by the micro-needle: 17%
- Friendly staff/supportive environment: 1%
- Availability/ease of access: 0%
- Effectiveness/flu coverage: 0%
- Other: 1%
- Not answered: 1%

Base: all subjects

Patient Acceptability study. Sanofi Pasteur, data on file.
Australia – Patient acceptability study

Intentions for next year’s flu vaccination

To be vaccinated with the same vaccine as today: 95%
To be vaccinated with IM vaccine: 2%
No vaccination: 1%
No preference: 0%
Not answered: 1%

Base: all subjects

Patient Acceptability study. Sanofi Pasteur, data on file.
Reaction of Australian GPs

• 7 in 10 GPs preferred the ID route

• Main reasons
  – Size / length of the needle
  – Innovative vaccine
  – Pain for the patient during / after injection
  – Safety for the vaccinator
  – Volume of antigen injected

• 95% of GPs would prescribe/administer again the intradermal flu vaccine next year
How satisfied are you with the vaccine you received today?

- Very Satisfied: 23.6%
- Satisfied: 73.9%
- Somewhat satisfied: 1.3%
- Not satisfied: 0.6%
- UNK: 0.6%

Database: total n = 157 surveys

Argentina – Patient acceptability study
Satisfaction with intradermal vaccine
Argentina – Patient acceptability study

Reasons for satisfaction with intradermal vaccine

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>The injection is not painful</td>
<td>69%</td>
</tr>
<tr>
<td>The administration process was quick</td>
<td>17%</td>
</tr>
<tr>
<td>I stayed calm because of the micro-needle (short and thin)</td>
<td>3%</td>
</tr>
<tr>
<td>Other</td>
<td>6%</td>
</tr>
<tr>
<td>UNK</td>
<td>5%</td>
</tr>
<tr>
<td>Total</td>
<td>156</td>
</tr>
</tbody>
</table>
Argentina – Patient acceptability study

Satisfaction with intradermal vaccine – ID vs. IM

Do you prefer the vaccine that you received today rather than the intramuscular vaccine?

- Yes: 88.50%
- No: 11.50%
For the next flu season, you might consider the following:

<table>
<thead>
<tr>
<th></th>
<th>Vaccination day</th>
<th>Phone call after one week</th>
</tr>
</thead>
<tbody>
<tr>
<td>To be vaccinated with the same vaccine I received today (ID)</td>
<td>83%</td>
<td>84%</td>
</tr>
<tr>
<td>To be vaccinated with an intramuscular needle</td>
<td>3%</td>
<td>4%</td>
</tr>
<tr>
<td>I would not get vaccinated</td>
<td>11%</td>
<td>8%</td>
</tr>
<tr>
<td>UNK</td>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Total N</td>
<td>157</td>
<td>147</td>
</tr>
</tbody>
</table>
IDflu® – Conclusions

- Using a simple and reliable Micro-Injection System, Sanofi Pasteur has developed the first intradermal seasonal influenza vaccine as an alternative to intramuscular vaccination.

- Clinical data
  - In adults 18-59 years
    - IDflu® 9 μg is as immunogenic as conventional 15 μg IM vaccine
  - In elderly people ≥60 years
    - Superior immunogenicity IDflu® 15 μg compared to conventional 15 μg IM vaccine
    - As immunogenic as an MF59 adjuvanted influenza vaccine

- First experiences from Australia and Argentina
  - Very well accepted by patients and doctors

- New alternative to IM vaccination could favor increased vaccine uptake
Thank you for your attention!

IDflu®
Influenza vaccine (split virion, inactivated)