Equivalent responses to quadrivalent influenza vaccine are detectable in blood and oral fluid in healthcare workers and men living with HIV on ART: findings from the FluAGE study

Megan E. Cole¹, Zainab Saeed¹, A. Torm Shaw¹, Yanping Guo², Katja Hoschler³, Alan Winston¹, Graham S. Cooke¹, Sarah Fidler¹, Graham P. Taylor¹,², and Katrina M. Pollock¹

k.pollock@imperial.ac.uk

¹Section of Virology, Department of Medicine, Imperial College London, London, UK. ²St. Mary's FACS facility, Imperial College London, London, UK. ³Respiratory Virus Unit, Virus Reference Department, National Infections Service, Public Health England, UK. ⁴Clinical Trials Centre, Jefferiss Wing, Imperial College Healthcare NHS Trust, London, UK.
A suboptimal response to influenza vaccine in PLWH despite ART?

HIV infection Worsens Age-Associated Defects in Antibody Responses to Influenza Vaccine

Varghese K. George, Suresh Pallikkuth, Anita Parmigiani, Maria Alcaide, Margaret Fischl, Kristopher L. Arheart, Savita Pahwa

Author Notes

The Journal of Infectious Diseases, Volume 211, Issue 12, 15 June 2015, Pages 1959–1968,

Impact of aging and HIV infection on serologic response to seasonal influenza vaccination

Pallikkuth, Suresh; De Armas, Lesley; R. Pathwa, Rajendra; Rinaldi, Stefano; George, Varghese, K.; Sanchez, Celeste; M. Rad, L.; Dickinson, Gordon; Rodriguez, Allan; Fischl, Margaret; Alcaide, Maria; Pathwa, Savita

Quadrivalent influenza vaccine is preferred for PLWH

© 2015 British HIV Association

British HIV Association guidelines on the use of vaccines in HIV-positive adults 2015

<table>
<thead>
<tr>
<th>Season</th>
<th>A/H1N1</th>
<th>A/H3N2</th>
<th>B</th>
<th>Additional B strain for QIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014/2015</td>
<td>A/California/7/2009</td>
<td>A/Texas/50/2012</td>
<td>B/Massachusetts/2/2/2012</td>
<td>N/A</td>
</tr>
<tr>
<td>2015/2016</td>
<td>A/California/7/2009</td>
<td>A/Switzerland/9715293/2013</td>
<td>B/Phuket/3073/2013</td>
<td>N/A</td>
</tr>
<tr>
<td>2016/2017</td>
<td>A/California/7/2009</td>
<td>A/HongKong/4801/2014</td>
<td>B/Brisbane/60/2008</td>
<td>N/A</td>
</tr>
</tbody>
</table>
FluAGE Study

Despite viral suppression with ART, is the cellular and antibody response to quadrivalent influenza vaccine compromised in men living with HIV infection?
1. Recruitment

Health Care Controls
- Men Living with HIV Infection
  - PBMC's
  - Thawed & aliquoted

4. Experiment design

16-parameter phenotypic staining for T and B cells subsets

2. Study Design

2017/18 Northern Hemisphere Influenza season

QIV*: administered post bleed

PBMCs collected

DAY 0

DAY 7

DAY 28

* Quadrivalent Influenza Vaccination

3. Sample processing

PBMC isolated

stored -150°C until use

5. Analysis using unsupervised algorithms

T-SNE
- FlowJo v10.4.2

SPADE
- FCS express v6plus

Images: Megan Cole
## Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>Control subjects</th>
<th>Early treated HIV</th>
<th>Chronic treated HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14 (100)</td>
<td>8 (100)</td>
<td>8 (100)</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White British</td>
<td>8 (57.1)</td>
<td>3 (37.5)</td>
<td>2 (25)</td>
</tr>
<tr>
<td>White Other</td>
<td>5 (35.7)</td>
<td>5 (62.5)</td>
<td>5 (62.5)</td>
</tr>
<tr>
<td>Black British</td>
<td>1 (7.2)</td>
<td>0 (0)</td>
<td>1 (12.5)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Median (IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37 (29-49)</td>
<td>48 (42-58)</td>
<td>50 (38-55)</td>
</tr>
<tr>
<td><strong>CD4 count at vaccination, cells/µl</strong></td>
<td>Median (IQR)</td>
<td>789 (665-1033)</td>
<td>609 (454-931)</td>
</tr>
<tr>
<td><strong>CD8 count at vaccination, cells/µl</strong></td>
<td>Median (IQR)</td>
<td>- -</td>
<td>720 (558-1034)</td>
</tr>
<tr>
<td><strong>CD4:CD8 ratio</strong></td>
<td>Median (IQR)</td>
<td>1 (0.91-1.41)</td>
<td>0.85 (0.61-1.21)</td>
</tr>
<tr>
<td><strong>Nadir CD4 count</strong></td>
<td>Median (IQR)</td>
<td>522 (466-734)</td>
<td>170 (80-410)</td>
</tr>
<tr>
<td><strong>HIV viral load at vaccination &lt;20 RNA copies/ml</strong></td>
<td>(%)</td>
<td>- -</td>
<td>8 (100)</td>
</tr>
<tr>
<td><strong>Duration HIV viral load suppressed (months)</strong></td>
<td>Median (IQR)</td>
<td>19 (6.8-26.5)</td>
<td>90 (53.0-159.0)</td>
</tr>
</tbody>
</table>

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Early treated HIV infection = individuals diagnosed with primary HIV infection and started on ART within three months (HEATHER)

Chronic treated HIV infection = individuals diagnosed and treated as part of routine clinical care
Antibody responses despite baseline seroprotection

Dark blue = seroprotection

Dark green = antibody response
Equivalent antibody protection in healthcare workers and PLWH

<table>
<thead>
<tr>
<th>Haemagglutination inhibition titre ≥40</th>
<th>Control subjects</th>
<th>Early treated HIV</th>
<th>Chronic treated HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>(%)</td>
<td>n</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>12</td>
<td>(85.7)</td>
<td>6</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>14</td>
<td>(100)</td>
<td>8</td>
</tr>
<tr>
<td>B/Brisbane</td>
<td>14</td>
<td>(100)</td>
<td>7</td>
</tr>
<tr>
<td>B/Phuket</td>
<td>14</td>
<td>(100)</td>
<td>8</td>
</tr>
</tbody>
</table>
Influenza/A-specific antibody in blood and oral fluid

Key: Control subjects - filled green circles; Early treated HIV – filled orange circles; Chronic treated HIV – open orange circles
Activation of circulating CD4+ T-follicular helper cells (cTFH) by quadrivalent influenza vaccination
Activation of circulating CD4+ T-follicular helper cells (cTFH) by quadrivalent influenza vaccination
Equivalent CD4+ T-helper cell (cTFH) response in PLWH and healthcare workers

Fold change equivalent in all groups studied p=0.89

Key: Control subjects - filled green circles; Early treated HIV – filled orange circles; Chronic treated HIV – open orange circles
Vaccination history in preceding three years

Key: Control subjects - filled green circles; Early treated HIV – filled orange circles; Chronic treated HIV – open orange circles

Cellular response
- cTFH PD-1+ICOS+CD38+
- Fold change GMT D28/D0
- PV=previously vaccinated
- NPV=not previously vaccinated

Humoral response
- Fold change GMT D28/D0
- p-values indicated for statistical significance
Conclusions

• First UK study of PLWH receiving the inactivated quadrivalent influenza vaccine

• High seroprotection rates, equivalent to those of healthcare workers, in men with suppressed HIV infection and immune recovery

• Findings support QIV in the seasonal influenza vaccination programme for PLWH

• Measurement of influenza-specific antibody in the mouth is a potential alternative to serum sampling

Under review Scientific Reports SREP-19-03442-T
E-Poster #319 Conference on Retroviruses and Opportunistic Infections, USA, 2019
Poster #025 Cole M et al. Responses to quadrivalent influenza vaccine reveal the landscape of CD32 expression on circulating T-follicular helper cells in men living with HIV infection.
Thank you

Graham Taylor
Sarah Fidler
Alan Winston
Graham Cooke
Yanping Guo
Jonathan Weber
Charles Bangham

HEATHER: HIV Reservoir targeting with Early Antiretroviral Therapy

POPPY: A Prospective, Observational Study to Examine the Effects of Ageing on the 'Pharmacokinetic and Clinical Observations in People Over Fifty'

Staff and patients of the Jefferiss Wing and the HIV Clinical Trials Centre