Vaccine Safety - What can we learn from...

Special Immunization Clinic

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1 March, 2023
Land acknowledgement

BC Children's Hospital Research Institute operates on the traditional, ancestral, and unceded territory of the Coast Salish peoples — xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Səl̓ílwətaʔ/Selilwitulh (Tsleil-Waututh) Nations.
BC Immunization Forum 2023 Presenter Disclosure

Manish Sadarangani

• Salary awards
  • BC Children’s Hospital Foundation
  • Michael Smith Foundation for Health Research

• Research/Project Funding
  • Merck, Moderna, VBI Vaccines, GlaxoSmithKline, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo

• All funds have been paid to my institute
• I have not received any personal payments
Mitigating Potential Bias

• No vaccine trade names or company names will be mentioned during the presentation, unless to provide clarity to aid audience understanding

• No off label recommendations will be made
My Brief

To be familiar with the contribution of the Special Immunization Clinics to research in vaccine safety including allergic events associated with COVID-19 vaccines
Vaccine safety: from population to molecule...

- Special Immunization Clinic (SIC) Network
Who are we?

- National team of expert clinicians
  - Infectious diseases
  - Allergy
  - Immunology
  - Hematology-Oncology
  - Transplant
  - Neurology

https://cirnetwork.ca/network/special-immunization/
What do we do?

• Standard patient assessments

• Evaluate vaccine safety in patients
  • With previous adverse events
  • With comorbidities that may affect vaccine response

• Ongoing studies
  • Optimizing management of patients with contraindication to vaccination and those with AEFI
  • Optimizing varicella immunization after transplant
  • Safety of rotavirus vaccination in infants born to people on ‘biologics’ (mAbs) during pregnancy

https://cirnetwork.ca/network/special-immunization/
Table III. Revaccination status and outcome of participants recommended and due for revaccination during the study period, stratified by AEFI type (N = 477)

<table>
<thead>
<tr>
<th>Revaccination status and outcome</th>
<th>Large local reaction N = 77 No. (%)</th>
<th>Other injection-site reaction* N = 19 No. (%)</th>
<th>Immediate hypersensitivity reaction† N = 101 No. (%)</th>
<th>Delayed hypersensitivity reaction and other allergic-like event‡ N = 76 No. (%)</th>
<th>Seizure N = 21 No. (%)</th>
<th>Other neurologic AEFI§ N = 21 No. (%)</th>
<th>Other systemic AEFI¶ N = 162 No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revaccination status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recorded revaccination</td>
<td>49 (64)</td>
<td>10 (53)</td>
<td>71 (70)</td>
<td>55 (72)</td>
<td>13 (62)</td>
<td>8 (38)</td>
<td>93 (57)</td>
</tr>
<tr>
<td>No recorded revaccination</td>
<td>28 (36)</td>
<td>9 (47)</td>
<td>30 (30)</td>
<td>21 (28)</td>
<td>8 (38)</td>
<td>13 (62)</td>
<td>69 (43)</td>
</tr>
<tr>
<td>Revaccination outcome</td>
<td>N = 49</td>
<td>N = 10</td>
<td>N = 71</td>
<td>N = 55</td>
<td>N = 13</td>
<td>N = 8</td>
<td>N = 93</td>
</tr>
<tr>
<td>AEFI recurrence</td>
<td>15 (31)</td>
<td>2 (20)</td>
<td>5 (7)</td>
<td>4 (7)</td>
<td>1 (8)</td>
<td>0 (0)</td>
<td>4 (4)</td>
</tr>
<tr>
<td>No AEFI recurrence</td>
<td>34 (69)</td>
<td>8 (80)</td>
<td>66 (93)</td>
<td>51 (93)</td>
<td>12 (92)</td>
<td>8 (100)</td>
<td>89 (96)</td>
</tr>
<tr>
<td>Severity relative to initial AEFI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milder</td>
<td>12 (80)</td>
<td>2 (100)</td>
<td>3 (60)</td>
<td>3 (75)</td>
<td>0 (0)</td>
<td>2 (50)</td>
<td></td>
</tr>
<tr>
<td>Same severity</td>
<td>1 (7)</td>
<td>0 (0)</td>
<td>1 (20)</td>
<td>1 (25)</td>
<td>0 (0)</td>
<td>1 (25)</td>
<td></td>
</tr>
<tr>
<td>More severe</td>
<td>2 (13)</td>
<td>0 (0)</td>
<td>1 (20)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (25)</td>
<td></td>
</tr>
<tr>
<td>Not reported</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (100)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

- Among 92 participants with suspected vaccine allergy who underwent skin testing and were revaccinated, the negative predictive value of skin testing for AEFI recurrence was 96% (95% CI 92.5%-99.5%)

Munoz et al. J Peds 2022
Patients with previous AEFI after COVID-19 vaccine

691 participants screened for COVID-19 AEFIs

- 211 not eligible
  - 17 eligibility undetermined
- 137 did not enrolled
  - 8 undetermined

463 participants eligible

- 137 did not enrolled
  - 8 undetermined
- 318 participants enrolled

Reason for referral
(Multiple can be selected)

- 145 Hypersensitivity reaction
- 41 Neurologic event
- 31 Hematologic disorder
- 77 Cardiac event
- 3 Acute organ dysfunction
- 31 Other Symptoms

Final AEFI diagnosis

- 110 Hypersensitivity reactions
- 72 Acute cardiac events
- 44 Neurologic events with a cute onset
- 31 Hematologic disorders
- 14 Other severe systemic AEFI
- 4 Severe large local infection
- 3 Acute onset organ dysfunction
- 0 Severe COVID-19 ≥2 weeks
- 40 Other AEFIs

Age

<table>
<thead>
<tr>
<th>Age</th>
<th>%</th>
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<tbody>
<tr>
<td>12-17 yo</td>
<td>17%</td>
</tr>
<tr>
<td>18-39 yo</td>
<td>30%</td>
</tr>
<tr>
<td>40-64 yo</td>
<td>44%</td>
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<tr>
<td>65+ yo</td>
<td>10%</td>
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</tbody>
</table>

Slide and data courtesy of Tiffany Fitzpatrick and Karina Top
Impact/Seriousness of AEFIs

Final AEFI Diagnosis

- Hypersensitivity reactions
- Neurologic events
- Hematologic disorders
- Acute cardiac events
- Acute onset organ dysfunction
- Severe large local reaction
- Other severe systemic AEFI
- Other AEFI

# Participants

- Low
- Moderate
- High
- Serious

Slide and data courtesy of Tiffany Fitzpatrick and Karina Top
Revaccination outcomes

Slide and data courtesy of Tiffany Fitzpatrick and Karina Top
Future/ongoing specific analyses

• Allergic-like events
  • To be presented at other meetings Spring 2023 (not yet public)

• Cardiac events
  • Data analysis ongoing

• Neurologic events
  • Data analysis ongoing
Varicella vaccine after solid organ transplant

**DEFER**
- Clinically unwell
- Current rejection
- High level immune suppression
- Recent or novel biologic use
- Underlying primary immunodeficiency
- Heart, Lung or Multivisceral transplant*

**POST TRANSPLANT**

**CAUTION**
- MMF
- History of ATG/Alemtuzumab/Rituximab
- Persistently elevated EBV
- Functional Tolerance

**VACCINATE**
- Ensure all timeline, immunosuppression & immune criteria are met
- Obtain informed consent
- Active & Passive surveillance mechanism for adverse events
- Consider two doses of VV and post vaccination serology to guide MMR doses

Suresh et al. Pediatr Transplant 2019
Rotavirus vaccine after in utero exposure to biologics

Clinical Care Pathway for infants exposed to monoclonal antibody biologics in utero

Public Health Unit, Primary Care provider, Pediatrician identifies eligible exposed infants (except certolizumab pegol)

Referral to local Special Immunization Clinic

Infliximab
Adalimumab
Golimumab

Infants required to combination therapy (i.e. CBT + Biologics) may be at increased risk of infection.

At INI (≤6 weeks)
- Retain newborn TREC if available
- CBC x 0.9
- Lymphocyte subsets (T, B, NK)
- Drug levels (Infliximab, Golimumab) ** to guide decision for rotavirus vaccine

Virtual visit at 6-12 months
- Review history and immunization history including potential AE/RF

Etanercept

At INI (≤6 weeks)
- Retain newborn TREC if available
- CBC x 0.9
- Lymphocyte subsets (T, B, NK)
- Drug levels ** to guide decision for rotavirus vaccine

Virtual visit at 6-12 months
- Review history and immunization history including potential AE/RF

Ustekinumab

At INI (≤6 weeks)
- Retain newborn TREC if available
- CBC x 0.9
- Lymphocyte subsets (T, B, NK)
- Drug levels ** to guide decision for rotavirus vaccine

Virtual visit at 6-12 months
- Review history and immunization history including potential AE/RF

Vedolizumab

At INI (≤6 weeks)
- Retain newborn TREC if available
- CBC x 0.9
- Lymphocyte subsets (T, B, NK)
- Drug levels ** to guide decision for rotavirus vaccine

Virtual visit at 6-12 months
- Review history and immunization history including potential AE/RF

Natalizumab

At INI (≤6 weeks)
- Retain newborn TREC if available
- CBC x 0.9
- Lymphocyte subsets (T, B, NK)
- Drug levels ** to guide decision for rotavirus vaccine

Virtual visit at 6-12 months
- Review history and immunization history including potential AE/RF

Rituximab
Belimumab

At INI (≤6 weeks)
- Retain newborn TREC if available
- CBC x 0.9
- Lymphocyte subsets (T, B, NK)
- Drug levels ** to guide decision for rotavirus vaccine

Virtual visit at 6-12 months
- Review history and immunization history including potential AE/RF

Additional Information:
- Partially resolved risk of infection with monoclonal biologics due to lack of other transfer of drug in utero
- CBC lymphopenia noted (not causal)
- Avoided drugs (see above)
- Drug levels (x 0.9) to be sent to Specimen at Level 3, or by hospital staff (special lot to be ordered) (Special consideration reported INI 3 working days)
- Examples: tocolactams, carbamazepine, valproic acid, azathioprine, cyclosporine

Abstract accepted for presentation at Canadian Immunization Conference 2023
INSIS brings together specialist clinicians, international experts in vaccine safety, systems biology, and genomics to characterize the clinical spectrum, risk factors, and underlying mechanisms of adverse events following COVID-19 immunization such as:

- Myocarditis
- Pericarditis
- Thrombosis with Thrombocytopenia Syndrome (TTS)
**SIC investigators**

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  - Méлина Denis
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  - Kim Simpson, Suganya Lee
  - Evgenia Tshaikovsky
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  - Chris Ireland
  - Barb Neufeld, Christine Bon
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  - Peter Ye
  - Melissa Moore, Project Manager
  - Dr. Tiffany Fitzpatrick

- **Funding**
  - Canadian Institutes of Health Research (CIHR)
  - IRSC (Institut de recherche sur les soins de santé)
  - CIHR IRSC (Institut de recherche sur les soins de santé, Canada)
  - Public Health Agency of Canada
  - Agence de santé publique du Canada
  - BC Children’s Hospital Research Institute
Thank you

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