COVID-19 Vaccines

BC Immunization Forum

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• Potential for conflict(s) of interest:
  • Dr. Langley’s employer, Dalhousie University, has received funding from Sanofi, GlaxoSmithKline, Moderna, Pfizer, Janssen, VIDO, VBI, whose product(s) are being discussed in this program. Dr. Langley holds the CIHR-GSK Chair in Pediatric Vaccinology at Dalhousie University.
Objectives:

• To be aware of the COVID-19 vaccine landscape
• To review use of vaccines in Canada and the world

Index case Dec 16, 2019

Published Date: 2019-12-30 13:59:03
Subject: PRO/AVH/EDR- Undiagnosed pneumonia - China (Hubei)

A: ProMED-mail post
http://www.promedmail.org

ProMED-mail is a program of the International Society for Infectious Diseases
http://www.isid.org

Dec 30, 2019

Index case Dec 16, 2019

Objective: Viral genome sequence posted on GENBANK and Virologic.org

• January 11, 2020: Pandemic declared by World Health Organization
• March 11, 2020: Pandemic declared by World Health Organization
• March 16: first patient enrolled in a phase 1 vaccine trial (mRNA-1273)
• July 2020: phase 3 trials begin, multiple platforms (mRNA, Ad vectored, protein based)
• Dec 14, 2020: COVID-19 vaccine program begins in Canada
WHO COVID vaccine target product profile

- Characteristics that are preferred or “critical or minimal”
- Target population – all ages (minimum adults including elderly)
- No contraindications (some e.g. immunocompromised possible)
- Safety/reactogenicity – favourable benefit/risk
- Efficacy ≥70% using endpoints of disease, severe disease; or ~50% point estimate of efficacy
- Single dose preferred
- Protection for at least 1 year (minimal 6 months)
- Capability to rapidly scale-up production at cost/dose that allows broad use including LMIC

Vaccines WHO Vaccines with Emergency Use authorization (EUA) Qualification

- mRNA
  - Moderna
  - Pfizer
- Adenovirus vectored
  - Janssen
  - AstraZeneca (Vaxevria and COVIDSHIELD)
- Protein subunit
  - Novavax (Nuvaxoid and Covovax)
- Inactivated
  - Sinovac
  - Sinophar/BIBP
  - Bharat Biotech

11 vaccines in evaluation
World Health Organization

Summary Information on Vaccine Products in Clinical Development

1. - Number of vaccines in clinical development: 145
2. - Number of vaccines in pre-clinical development: 195

Abandoned vaccines

- mRNA
  - Imperial College Morningside sRNA Jan 27, 2021 “not the time to start an efficacy trial” and “not a satisfying immune response” [https://doi.org/10.1016/j.eclinm.2021.101262](https://doi.org/10.1016/j.eclinm.2021.101262) (phase 1)
  - Curevac mRNA; 48% efficacy in phase 3 trial; “pandemic window closing”; focussing on 2nd generation vaccine

- DNA
  - Oncosec CORVax12 protein plasmid DNA vaccine (codes for spike and IL-12) phase 1 in Jan 2021, abandoned Nov 2021 [NCT04627675](https://clinicaltrials.gov/ct2/show/NCT04627675)

- Virus vectored
  - Merck/Themis Bioscience/Institut Pasteur (measles virus vector) phase 1 trial results weaker than natural infection
  - Merck/IAVI viral vector (vesiculostomatitis virus) phase 1 trial results weaker than natural infection [NCT04569786](https://clinicaltrials.gov/ct2/show/NCT04569786)
  - Alimmune AdCOVID nasal spray Ad5 phase 1; substantially lower antibody levels that authorized vaccines [NCT04679909](https://clinicaltrials.gov/ct2/show/NCT04679909)

- Protein subunit
  - University of Queensland CSL MF59 adjuvanted, stabilized in pre-fusion conformation with a novel molecular clamp (sclamp) 99% had nAB; false positive HIV tests [https://dx.doi.org/10.2139/ssrn.3769210](https://dx.doi.org/10.2139/ssrn.3769210)
  - RIBSP QazCoVac-P subunit vaccine Kazakhstan [NCT04930003](https://clinicaltrials.gov/ct2/show/NCT04930003)
  - SK bioscience South Korea NBP2001 phase 1 completed

- Inactivated
  - Iran Ministry of Defence inactivated coronavirus vaccine, Fakhrvac
COVID-19 vaccines procured by Government of Canada

- Lipid Nanoparticle-messenger RNA (mRNA)
  - Moderna 56 M doses
  - Pfizer-BioNTech 80 M doses
- Viral vector (adenovirus)
  - Janssen (Johnson and Johnson) 38 M doses
  - AstraZeneca-Oxford 20 M doses
- Subunit protein, adjuvanted
  - Novavax 76 M doses (approved Feb 2022)
  - Sanofi Pasteur – GSK 72 M doses (approval pending, rolling submission)
- Virus-like particle
  - Medicago 76M doses (approved Feb 2022)

COVAX

- Vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator, launched April 2020 by WHO, European Commission, France; now led by CEPI, GAVI, UNICEF, WHO
  - Goal is to accelerate development, production, and access
  - Global risk-sharing mechanism for pooled procurement equitable access to vaccines
  - Doses for at least 50% of global population
  - Diverse and actively managed portfolio of vaccines
  - Options for countries:
    - Committed purchase
      - Lower upfront payment
      - Purchase allocated vaccines
    - Optional purchase
      - Larger upfront payment
      - Purchase vaccine of choice

CEPI, Gavi, UNICEF, WHO
Share of world's population receiving at least one dose

Cumulative percentage of Canadians who have received a COVID-19 vaccine by age group and report week, Feb 20, 2022


https://health-infobase.canada.ca/covid-19/vaccination-coverage/#a5
Cumulative percentage of people who are fully vaccinated (two doses) with a COVID-19 vaccine in Canada by age group and report week Feb 2022

<table>
<thead>
<tr>
<th>Vaccine series</th>
<th>Vaccine included in the vaccine series</th>
<th>At least 1 dose</th>
<th>Partially vaccinated</th>
<th>Fully vaccinated</th>
<th>Fully vaccinated with an additional dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homologous priming (1,2):</td>
<td>Pfizer-BioNTech Comirnaty</td>
<td>1,880,475 (33.64%)</td>
<td>1,665,020 (29.80%)</td>
<td>1,238,840 (22.32%)</td>
<td>5,805,070 (10.19%)</td>
</tr>
<tr>
<td>Homologous priming (1,2):</td>
<td>Moderna Spikevax</td>
<td>1,002,576 (18.24%)</td>
<td>935,344 (16.76%)</td>
<td>571,829 (10.75%)</td>
<td>1,847,739 (3.32%)</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Astrazeneca Vaxzevria/COVSHIELD</td>
<td>198,705 (3.54%)</td>
<td>139,084 (2.48%)</td>
<td>105,090 (1.92%)</td>
<td>664 (0.01%)</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Janssen</td>
<td>30,859 (0.56%)</td>
<td>24 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Non-Health-Canada-approved vaccines</td>
<td>15,158 (0.27%)</td>
<td>5,380 (0.09%)</td>
<td>6,008 (0.12%)</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Other Pfizer-BioNTech Comirnaty vaccine with the Moderna Spikevax vaccine</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Other Pfizer-BioNTech Comirnaty vaccine with the Moderna Spikevax vaccine or Moderna Spikevax</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Other Moderna Spikevax with mRNA vaccine (either Pfizer-BioNTech Comirnaty vaccine or Moderna Spikevax)</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Novavax Nuvaxovid with an mRNA vaccine (either Pfizer-BioNTech Comirnaty vaccine or Moderna Spikevax)</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Janssen with other Health Canada-approved vaccines</td>
<td>5,461 (0.02%)</td>
<td>8,451 (0.02%)</td>
<td>7,377 (0.02%)</td>
<td></td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Other Health Canada-approved vaccines</td>
<td>40,554 (0.11%)</td>
<td>6,461 (0.02%)</td>
<td>8,959 (0.02%)</td>
<td></td>
</tr>
<tr>
<td>Heterologous priming (1,2):</td>
<td>Other</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Homologous priming (1,2): ~33% Pfizer ~10% Moderna
Heterologous priming (1,2): ~13% 2 mRNA's ~4% AZ followed by mRNA

https://health-infobase.canada.ca/covid-19/vaccination-coverage/#a5
COVID-19 cases by vaccination status

- Authorized vaccines were highly effective in randomized controlled trials leading to their approval
- Vaccine effectiveness against severe outcomes was good to excellent during Delta, Omicron
- Vaccine effectiveness against “infection” is low to absent during Omicron period
An analytic framework for immunization
(after United States Task Force on Preventive Health Care)

How correlates are determined

• Levels of passively administered or maternal antibody that protect
• Analysis of immune responses in protected and unprotected subjects in efficacy trials
• Observations made on vaccine failures, e.g. immunocompromised patients
• Human challenge studies
• Extrapolation from animal challenge studies, including immunodeficiency
Potential protective adaptive immune mechanisms induced by vaccination

- Serum antibody
  - Neutralizing
  - Non-neutralizing (ADCC, etc)
  - Functionality (opsonophagocytosis)
  - Avidity
- Mucosal antibody
  - IgA locally produced
  - IgG produced from serum
- CD4+ T cells
  - B cell helper
  - T cell helper
  - Th17
  - Cytokines
  - Lysis
  - Tregs
- CD8+ cells
  - Lysis
  - Avidity

Summary: COVID-19 vaccines

- Highly effective vaccines were developed rapidly during the COVID-19 vaccine pandemic
- Canada did not develop a vaccine to mitigate the high incidence periods of the pandemic, but now has the potential to domestically produce at least one vaccine, potentially three vaccines
- Remaining questions:
  - What outcomes do we want to prevent?
  - Which useful correlates of protection will be accepted?
  - What will be the vaccine schedule in the future?