

## COVID-19 Vaccine Bulletin #6

### Viral Vector Vaccines

The purpose of the Vaccine Bulletin is to give you the latest information about COVID-19 vaccines. For this bulletin, the focus will be on the viral vector vaccines that are the next front-runners for vaccine approval in Canada.

#### **Quick Updates:**

- WDGPH will begin immunizing residents in long term care and retirement homes on Thursday January 14, 2021.
- There is an [attestation form](#) available for clients who have special medical considerations. This form is signed by the client.
- Please visit our website for detailed vaccine information and links to guidance documents, educational material and webinars for healthcare providers at: <https://www.wdgppublichealth.ca/healthcare-providers/covid-19-information-healthcare-providers/covid-19-vaccine-information>

### **Viral Vector Vaccines**

The table below highlights the two viral vector vaccines that are currently under review by Health Canada.

| Vaccine Developer                                       | AstraZeneca/Oxford                              | Janssen Pharmaceutical/<br>Johnson & Johnson |
|---|---|--|
| <b>Vaccine Platform</b>                                 | Viral vector (non-replicating)                  | Viral vector (non-replicating)               |
| <b>Storage Needs</b>                                    | 2-8°C for six months                            | 2-8°C for three months                       |
| <b>No. of Doses</b>                                     | 2   | 1-2  |
| <b>Timing of Doses</b>                                  | 28 days apart                                   | 56 days apart                                |
| <b>Route of Admin.</b>                                  | Intramuscular injection                         | Intramuscular injection                      |
| <b>Application to Health Canada</b>                     | 10-01-2020                                      | 11-30-2020                                   |
| Based on Phase 1/2 studies and preliminary phase 3 data |   |  |
| <b>Effectiveness</b>                                    | 62 to 90% effective depending on initial dosage | TBD  |
| <b>Side effects</b>                                     | Pain, fatigue, headache                         | Fever, fatigue, headache, myalgia            |
| <b>Safety</b>   | No serious safety concerns                      | No serious safety concerns                   |

## **What are Viral Vector Vaccines?**

- Viral vector vaccines use a modified **adenovirus (vector)** that prompts an immune response to COVID-19 in the body
- An adenovirus is a common virus that typically causes cold and flu-like symptoms. Researchers have developed an adenovirus that contains the DNA for the spike protein that surrounds the SARS-CoV-2 virus but does not replicate.
- The modified **adenovirus** pushes its DNA into the cell and creates messenger RNA (mRNA). The cell reads the mRNA and creates the SARS-CoV-2 spike proteins.
- The adenovirus and the spike protein cause an immune response in the body which protects a person from getting ill with COVID-19.
- Viral vector technology has been used to develop many vaccines for animals and is also an emerging technology for use in human vaccines, including an Ebola vaccine

## **Vaccine Safety & Efficacy (Results of Preliminary Trials)**

### **AstraZeneca/Oxford**

[Folegatti et al.](#) did a phase 1/2, single-blind, randomised controlled trial in five trial sites in the UK of a chimpanzee adenovirus-vectored vaccine (ChAdOx1 nCoV-19; **AstraZeneca/Oxford**) expressing the SARS-CoV-2 spike protein compared with a meningococcal conjugate vaccine (MenACWY) as control. Healthy adults aged 18–55 years with no history of laboratory confirmed SARS-CoV-2 infection or of COVID-19-like symptoms were randomly assigned to receive ChAdOx1 nCoV-19 at a dose of  $5 \times 10^8$  viral particles or MenACWY as a single intramuscular injection. A protocol amendment in two of the five sites allowed prophylactic paracetamol to be administered before vaccination. Ten participants assigned to a non-randomised, unblinded ChAdOx1 nCoV-19 prime-boost group received a two-dose schedule, with the booster vaccine administered 28 days after the first dose. The authors report the preliminary findings on safety, reactogenicity, and cellular and humoral immune responses.

*Findings:* Between April 23 and May 21, 2020, 1077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534) (control), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group. Local and systemic reactions were more common in the ChAdOx1 nCoV-19 group and many were reduced by use of prophylactic paracetamol, including pain, feeling feverish, chills, muscle ache, headache, and malaise (all  $p < 0.05$ ). There were no serious adverse events related to ChAdOx1 nCoV-19. In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14 (median 856 spot-forming cells per million peripheral blood mononuclear cells, IQR 493–1802; n=43). Anti-spike IgG responses rose by day 28 (median 157 ELISA units [EU], 96–317; n=127), and were boosted following a second dose (639 EU, 360–792; n=10). Neutralising antibody responses against SARS-CoV-2 were detected in 32 (91%) of 35 participants after a single dose when measured in MNA80 and in 35 (100%) participants when measured in PRNT50.

After a booster dose, all participants had neutralising activity (nine of nine in MNA80 at day 42 and ten of ten in Marburg VN on day 56). Neutralising antibody responses correlated strongly with antibody levels measured by ELISA ( $R^2=0.67$  by Marburg VN;  $p<0.001$ ).

*Interpretation:* ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses. These results, together with the induction of both humoral and cellular immune responses, support large-scale evaluation of this candidate vaccine in an ongoing phase 3 programme.

### **Janssen/Johnson & Johnson**

[Sadoff et al.](#) conducted a multi-center phase 1/2a randomized, double-blinded, placebo-controlled clinical study to assess the safety, reactogenicity and immunogenicity of Ad26.COV2.S (**Johnson & Johnson**), a non-replicating adenovirus 26 based vector expressing the stabilized pre-fusion spike (S) protein of SARS-CoV-2. Ad26.COV2.S was administered at a dose level of  $5 \times 10^{10}$  or  $1 \times 10^{11}$  viral particles (vp) per vaccination, either as a single dose or as a two-dose schedule spaced by 56 days in healthy adults (18-55 years old; cohort 1a & 1b;  $n=402$  and healthy elderly  $>65$  years old; cohort 3;  $n=394$ ). Vaccine elicited S specific antibody levels were measured by ELISA and neutralizing titers were measured in a wild-type virus neutralization assay (wtVNA). CD4+ T-helper (Th)1 and Th2, and CD8+ immune responses were assessed by intracellular cytokine staining (ICS).

*Results:* In cohorts 1 and 3 solicited local adverse events were observed in 58% and 27% of participants, respectively. Solicited systemic adverse events were reported in 64% and 36% of participants, respectively. Fevers occurred in both cohorts 1 and 3 in 19% (5% grade 3) and 4% (0% grade 3), respectively, were mostly mild or moderate, and resolved within 1 to 2 days after vaccination. The most frequent local adverse event (AE) was injection site pain and the most frequent solicited AEs were fatigue, headache and myalgia. After only a single dose, seroconversion rate in wtVNA (50% inhibitory concentration - IC50) at day 29 after immunization in cohort 1a already reached 92% with GMTs of 214 (95% CI: 177; 259) and 92% with GMTs of 243 (95% CI: 200; 295) for the  $5 \times 10^{10}$  and  $1 \times 10^{11}$  vp dose levels, respectively. A similar immunogenicity profile was observed in the first 15 participants in cohort 3, where 100% seroconversion (6/6) (GMTs of 196 [95%CI: 69; 560]) and 83% seroconversion (5/6) (GMTs of 127 [95% CI: <58; 327]) were observed for the  $5 \times 10^{10}$  or  $1 \times 10^{11}$  vp dose level, respectively. Seroconversion for S antibodies as measured by ELISA (ELISA Units/mL) was observed in 99% of cohort 1a participants (GMTs of 528 [95% CI: 442; 630] and 695 (95% CI: 596; 810]), for the  $5 \times 10^{10}$  or  $1 \times 10^{11}$  vp dose level, respectively, and in 100% (6/6 for both dose levels) of cohort 3 with GMTs of 507 (95% CI: 181; 1418) and 248 (95% CI: 122; 506), respectively. On day 14 post immunization, Th1 cytokine producing S-specific CD4+ T cell responses were measured in 80% and 83% of a subset of participants in cohort 1a and 3,

respectively, with no or very low Th2 responses, indicative of a Th1-skewed phenotype in both cohorts. CD8+ T cell responses were also robust in both cohort 1a and 3, for both dose levels.

*Conclusions:* The safety profile and immunogenicity after only a single dose are supportive for further clinical development of Ad26.COVS.2 at a dose level of 5x10<sup>10</sup> vp, as a potentially protective vaccine against COVID-19.

## References

*Note: Because of the emerging and currently evolving nature of scientific information on SARS-CoV-2/COVID-19 vaccines, some of the scientific reports listed here may not have been peer-reviewed or may have been subjected only to an expedited peer-review process. Conclusions may change as further information becomes available and should therefore not necessarily be accepted as established.*

Folegatti PM, Ewer KJ, Aley PK et al. [Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial.](#) Lancet. 2020; (published online July 20.) DOI: [https://doi.org/10.1016/S0140-6736\(20\)31604-4.](https://doi.org/10.1016/S0140-6736(20)31604-4)

Sadoff J, Le Gars M, Shukarev G, et al. [Safety and immunogenicity of the Ad26.COVS.2 COVID-19 vaccine candidate: interim results of a phase 1/2a, double-blind, randomized, placebo-controlled trial.](#) MedRxiv Sep 20, 2020.  
DOI: <https://doi.org/10.1101/2020.09.23.20199604>

World Health Organization (2020). [Draft landscape of COVID-19 candidate vaccines.](#)

AstraZeneca (November 23, 2020). [AZD1222 vaccine met primary efficacy endpoint in preventing COVID-19.](#)

Johnson & Johnson (January 5, 2021). [COVID-19 update: Your latest questions about Johnson & Johnson's investigational vaccine candidate answered.](#)

## Ministry of Health Vaccine Guidance

Please note the updates (January 12) to the Ministry of Health [COVID-19 vaccine-relevant information and planning resources](#) posted on their website on their website. Of special note is the addition of two guidance documents:

- [COVID-19 Recommendations for Special Populations](#)  
This document provides recommendations on vaccine administration for special populations such as those who are pregnant, breastfeeding, have autoimmune conditions or are immunocompromised, or have severe allergies. The document will be regularly updated as COVID-19 vaccines are authorized for use in Canada, and as evidence on these vaccines evolve.
- [COVID-19: Guidance for Prioritizing Health Care Workers for COVID-19 Vaccination](#)  
This document provides guidance for a stepwise approach to health care worker prioritization focusing first on sectors and settings, then on level of community risk, and lastly on individual risk.

### ***Status of Doses Administered in Ontario***

Total doses administered = 144,784

Daily doses administered = 11,231

Total vaccinations completed = 8,778

Total doses administered in **Wellington-Dufferin-Guelph** = 1,019

## COVID-19 Vaccine Webinars for Health Care Providers

***The COVID-19 Pivot: Vaccine Update for Family Physicians*** (College of Family Physicians of Canada) <https://www.youtube.com/watch?v=MehpXnRvFG0> (Jan. 12, 2021)

***Changing the Way We Work: Update on COVID-19 Vaccines*** (Ontario College of Family Physicians) [https://www.youtube.com/watch?v=YaltNQczl6Y&feature=emb\\_title](https://www.youtube.com/watch?v=YaltNQczl6Y&feature=emb_title) (Jan. 8, 2021)

## Reliable Sources of Information on Vaccines

[Public Health Agency of Canada](#)

[Government of Ontario](#)

[Public Health Ontario](#)

[Centre for Effective Practice \(CEP\)](#)

[World Health Organization](#)

[COVID-19 Studies from the World Health Organization Database](#)

[Centres for Disease Control and Prevention \(CDC\)](#)