COVID-19 Vaccine Bulletin #1

The purpose of the Vaccine Bulletins is to give you the latest information about COVID-19 vaccines. Due to the ever-changing landscape of vaccine research and distribution it is expected that this information will need to be updated frequently. Wellington-Dufferin-Guelph Public Health (WDGPH) will keep you up-to-date on the information as it becomes available to us.

For this bulletin, the focus will be on two vaccine front-runners for use in Canada:

1. BioNTech/Fosun Pharma/Pfizer (mRNA)
2. Moderna/NIAID (mRNA)

Vaccine Summary Table

Vaccine Developer	BioNTech/Fosun Pharma/Pfizer	Moderna/NIAID
Vaccine Platform	RNA	RNA
Type of Candidate Vaccine	3 LNP-mRNAs	LNP-encapsulated mRNA
Storage Needs	-75C Refrigerator (up to 5 days)	-20C Refrigerator (up to 30 days)
No. of Doses	2	2
Timing of Doses	21 days apart	28 days apart
Route of Admin.	Intramuscular injection	Intramuscular injection
Distribution Plan	TBD	TBD
Based on Phase 1/2 studies and preliminary phase 3 data		
Effectiveness	95% effective across diverse subgroups	94.5% effective across diverse subgroups
Side effects	Pain, fatigue, headache	Injection site pain, fatigue, headache, pain, redness at injection site
Safety	No serious safety concerns	No serious safety concerns

What are messenger RNA (mRNA) vaccines?

- Messenger RNA are strands of genetic material that direct protein production in cells.
- Scientists have developed mRNA that directs cells to produce proteins that imitate those found in SARS-CoV-2.
- When the mRNA vaccine is injected into the body, the cells use it to make viral proteins (antigens).
- The viral proteins trigger immune cells which lead to the production of antibodies.
- In the past, mRNA technology has been focused on cancer, with tumour mRNA being used to help people's immune systems recognise and respond to the proteins produced by their specific tumours.
- mRNA vaccines are a promising alternative to conventional vaccine approaches because of high potency and the capacity for rapid and safe administration.
- mRNA vaccines to date, come with logistical challenges for delivery due to vaccine storage and handling requirements needed to keep the vaccine stable.

Peer Reviewed and Pre-print (non-peer-reviewed) Articles

Chung et al. provide a review of the front-runners in vaccine development including the results of their early trials while highlighting the role of the nanotechnologies used by all the vaccine developers.

Vaccine Safety (Preliminary Trials)

Jackson et al., conducted a phase 1, dose-escalation, open-label trial including 45 healthy adults, who received two vaccinations, 28 days apart, with mRNA-1273 in a dose of 25 µg, 100 µg, or 250 µg (**Moderna** vaccine). After the first vaccination, antibody responses were higher with higher dose and increased after the second dose. The mRNA-1273 vaccine induced anti–SARS-CoV-2 immune responses in all participants, and no trial-limiting safety concerns were identified. Solicited adverse events that occurred in more than half the participants included fatigue, chills, headache, myalgia, and pain at the injection site. Systemic adverse events were more common after the second vaccination, particularly with the highest dose, and three participants (21%) in the 250-µg dose group reported one or more severe adverse events.

The two-dose vaccine series was generally without serious toxicity; systemic adverse events after the first vaccination, when reported, were all graded mild or moderate. Greater reactogenicity followed the second vaccination, particularly in the 250-µg group.

Across the three dose groups, local injection-site reactions were primarily mild. This descriptive safety profile is similar to that described in a report of two trials of avian influenza mRNA vaccines (influenza A/H10N8 and influenza A/H7N9) that were manufactured by Moderna with the use of an earlier lipid nanoparticle capsule formulation11 and is consistent with an interim report of a phase 1–2 evaluation of a Covid-19 mRNA vaccine encoding the S receptor-binding domain. Those studies showed that solicited systemic adverse events tended to be more frequent and more severe with higher doses and after the second vaccination.

Mulligan et al. report the available safety, tolerability, and immunogenicity data from an ongoing placebo-controlled, observer-blinded dose escalation study among healthy adults, 18-55 years of age, randomized to receive 2 doses, separated by 21 days, of 10 µg, 30 µg, or 100 µg of BNT162b1, a lipid nanoparticle-formulated, nucleoside-modified, mRNA vaccine that encodes trimerized SARS-CoV-2 spike glycoprotein RBD (**Pfizer** vaccine). Local reactions and systemic events were dose-dependent, generally mild to moderate, and transient. RBD-binding IgG concentrations and SARS-CoV-2 neutralizing titers in sera increased with dose level and after a second dose. Geometric mean neutralizing titers reached 1.8- to 2.8-fold that of a panel of COVID-19 convalescent human sera. These results support further evaluation of this mRNA vaccine candidate.

From Chung et al.: Both BioNTech/Pfizer and Moderna released encouraging safety and immunogenicity data. Moderna tested a higher range of mRNA (25, 100, and 250 µg), while BioNTech/Pfizer tested 10, 30, and 100 µg. Safety evaluations noted no severe adverse events that warranted the discontinuation of either trial. Some of the more prominent adverse events in the Moderna trial included pain, headache, and chills, while BioNTech/Pfizer's vaccine mainly caused pain, fatigue, and headache. Antibody response was also positive in both trials. Moderna tested antibody response through ELISA assays while BioNTech/Pfizer utilized a RBD-binding IgG assay.17,19 For Moderna, when comparing the response in vaccinated patients to convalescent serum from past SARS-CoV-2 patients, the 250 µg group generated higher S-2P geometric mean titers (GMTs) by day 15 (163,449 vs 142,140 arbitrary units (AU)), while the 25 and 100 µg groups produced higher GMTs by day 36 (391,018 and 781,399 AU, respectively), 7 days after a second boost. BioNTech/Pfizer recorded neutralizing anti-RBD titers much higher than convalescent serum levels. By day 21 (day of the second dose, or 21 days), the 30 µg group had a higher geometric mean concentration (GMC) than convalescent sera (1,536 vs 602 U/mL), while it took until day 28 (7 days after a second dose) for the 10 µg group (4,813 U/mL). The 100 µg group, which only used one dose, had higher GMC levels by day 21 (1,778 U/mL). Both Moderna and BioNTech/Pfizer tested T-cell responses and demonstrated TH1 skewed T-cell responses with detectable CD4+ and CD8+ response to their respective antigens.17,20 Neither developer mentioned the production of antibodies other than IgG. It is difficult to directly compare the results between the trials because

measurements and data reporting are not standardized, highlighting an opportunity and need to standardize vaccine trials and reporting requirements.

The vaccination schedule in the Phase III trials by both Moderna and BioNTech/Pfizer will not deviate from their Phase II setups. Moderna will continue to boost on day 29 after an initial injection, and BioNTech/Pfizer will boost at day 21. However, Phase III trials will only evaluate one dose. In Moderna's case, the midlevel dose led to higher immunogenicity than the highest dose while BioNTech/Pfizer demonstrated no substantial differences between their mid- and high-level doses. Therefore, Moderna and BioNTech/Pfizer both chose to move forward with their midlevel doses (100 µg and 30 µg, respectively). For phase III, Moderna and BioNTech/Pfizer will also vaccinate much larger populations of 30,000 participants each.

Vaccine Hesitancy

Gadoth et al. conducted a cross-sectional survey among 1,093 volunteer-sampled University of California, Los Angeles (UCLA) Health System employees between September 24 and October 16, 2020, of which 609 participated. They found respondents overwhelmingly confident about vaccine safety (4.47 out of a 5-point scale); effectiveness (4.44); importance, self-protection, and community health (4.67). However, 47.3% of respondents reported unwillingness to participate in a coronavirus vaccine trial, and most (66.5%) intended to delay vaccination. The odds of reporting intent to delay coronavirus vaccine uptake were 4.15 times higher among nurses, 2.45 times higher among other personnel with patient contact roles, and 2.15 times higher among those without patient contact compared to doctors. Evolving SARS-CoV-2 science (76.0%), current political climate (57.6%), and fast-tracked vaccine development timeline (83.4%) were cited as primary variables impacting HCW decisions to undergo vaccination. Of note, these results were obtained prior to release of Phase III data from companies manufacturing vaccines in the U.S.

References

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

Press releases (Phase III)

Pfizer (November 18, 2020). Pfizer and BioNTech conclude phase study of COVID-19 vaccine candidate, meeting all primary efficacy endpoints.

Moderna (November 16, 2020). Moderna's COVID-19 vaccine candidate meets its primary efficacy endpoint in the first interim analysis of the phase 3 COVE study.

Published Scientific Articles

Note: Because of the emerging and currently evolving nature of scientific information on SARS-CoV-2/COVID-19, 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.

Chung YH, Beiss V, Fiering SN and Steinmetz NF. COVID-19 Vaccine Frontrunners and Their Nanotechnology Design. ACS Nano. 2020 Oct 27;14(10):12522-12537. doi: 10.1021/acsnano.0c07197. Epub 2020 Oct 9. PMID: 33034449 PMCID: PMC7553041 DOI: 10.1021/acsnano.0c07197

Gadoth A, Halbrook M, Martin-Blais R, et al. Assessment of COVID-19 vaccine acceptance among healthcare workers in Los Angeles. MedRxiv 2020.11.18.20234468; doi: https://doi.org/10.1101/2020.11.18.20234468

Jackson LA, Anderson EJ, Rouphael NG, et al. An mRNA Vaccine against SARS-CoV-2 — Preliminary Report. N Engl J Med 2020; 383:1920-1931 DOI: 10.1056/NEJMoa2022483

Mulligan MJ, Lyke KE, Kitchin N, et al. Phase 1/2 Study to Describe the Safety and Immunogenicity of a COVID-19 RNA Vaccine Candidate (BNT162b1) in Adults 18 to 55 Years of Age: Interim Report. MedRxiv 2020.06.30.20142570; doi: https://doi.org/10.1101/2020.06.30.20142570