COVID-19 Vaccines: mRNA Vaccines

Introduction

The novel coronavirus disease (COVID-19) pandemic has stimulated unprecedented efforts to develop vaccines that provide protection against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).\(^1\)

This Focus On is the first in a series on emerging COVID-19 vaccines, intended for health care providers and public health partners. It provides an overview of messenger ribonucleic acid (mRNA) vaccines, including products undergoing regulatory review or authorized for use in Canada. Given the rapidly evolving state of COVID-19 vaccine development, this document will be updated as new information becomes available.

The basics: mRNA vaccines

mRNA vaccines have emerged as a promising alternative to conventional vaccine platforms.\(^2,3\) While efforts to develop an mRNA vaccine were initially limited by the transient nature of mRNA in human cells, major innovations over the last two decades have accelerated mRNA vaccine development.\(^2-4\)

What is mRNA?

Messenger ribonucleic acid (mRNA) is a type of transcript, which is used by our cells to transfer genetic information from DNA to make proteins.\(^2,5-7\)

Vaccines work by training our immune system to recognize and respond to infectious agents. Normally, this is accomplished by delivering a weakened or inactivated virus or a component of the virus (such as a specific protein) to the body, which triggers an immune response.\(^2,3\) In contrast, mRNA vaccines work by delivering instructions to human cells to produce a viral protein, which is then recognized by the body as foreign.\(^2,8\) These proteins, known as antigens, use the body’s normal processes to safely produce an immune response. There are two main types of RNA vaccines:

- **Non-replicating (or non-amplifying) RNA vaccines** are the simplest type consisting of mRNA coding for the viral antigen. Our cell machinery is used to make viral antigen and once this is accomplished, the mRNA is cleared.\(^9,10\) COVID-19 mRNA vaccines are non-replicating RNA vaccines.\(^3,10\)

- **Self-replicating (or self-amplifying) RNA vaccines** consist of an RNA coding for the viral antigen and the virus’ replication machinery, allowing for abundant production of viral antigen.\(^9,10\)
Mechanism of action and immune response

COVID-19 mRNA vaccines use our normal cell processes to safely produce the SARS-CoV-2 spike glycoprotein antigen, which activates both antibody and cell-mediated immune responses.\(^7,10,11\)

- mRNA vaccines are encapsulated in a lipid coat, commonly referred to as a lipid nanoparticle (LNP), which allows them to easily cross cell membranes and into the cells.\(^2-7\)
- Once inside our cells, mRNA is released into the cytoplasm where the body’s cell machinery makes copies of the SARS-CoV-2 spike glycoprotein antigen. The mRNA instructions are then rapidly broken down and disposed of by our cells.\(^3-7,10,11\)
- Next, the SARS-CoV-2 spike glycoprotein antigen is temporarily displayed on the surface of our cells where it activates B (antibody-mediated) and T (cell-mediated) cells of the immune system.\(^3,10,11\)
- Activation of cell-mediated immune responses are expected to play a central role in providing us with long-term protection.\(^10\) Antibody-mediated responses directed against the SARS-CoV-2 spike glycoprotein are believed to be important for blocking the virus from entering our cells.\(^10\)

Key messages: COVID-19 mRNA vaccines

1. You cannot get COVID-19 from an mRNA vaccine

mRNA COVID-19 vaccines are non-infectious (they do not contain whole or live SARS-CoV-2); therefore there is no risk of an mRNA vaccine causing infection with COVID-19.\(^3-7\)

2. mRNA vaccines are a new vaccine platform, but not a new technology

While mRNA therapeutics have been studied for over two decades, recent scientific advancements have improved mRNA stability and delivery which has been important for bringing mRNA vaccines and cancer mRNA therapeutics into clinical use.\(^2,4,6,7\)

3. mRNA vaccines do not affect or interact with our DNA

Human cells break down and get rid of mRNA as soon as they finish using its instructions. mRNA does not enter the nucleus of human cells, where our DNA is located, eliminating any risk of mRNA interacting with our DNA.\(^2-7,11\)

Advantages and limitations of mRNA vaccines

Recent advances in mRNA vaccine technology offer several advantages over classical vaccine platforms. Rapid and scalable manufacturing as compared to conventional vaccines, allows for quicker vaccine production in response to novel pathogens such as SARS-CoV-2.\(^3,4,11\) Additionally, since mRNA vaccines produce both antibody and cell-mediated immune system responses they are anticipated to provide longer-term protection.\(^10\) Finally, mRNA vaccines are non-infectious so there is no risk of infection from the vaccine.\(^3-7,11\) Limitations of mRNA vaccine use relate to vaccine storage and handling requirements,
including the need for freezing temperatures and increased reactogenicity (i.e. side effects such as fever, muscle aches and fatigue), relative to some other vaccine platforms.\textsuperscript{3-5,11-13}

**COVID-19 mRNA vaccines**

In Canada, one COVID-19 mRNA vaccine has been approved for use with another one currently being reviewed, under Health Canada’s *Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19*.\textsuperscript{5} Detailed characteristics of each vaccine are outlined in Table 1.

**Table 1: Characteristics of COVID-19 mRNA vaccines**

<table>
<thead>
<tr>
<th></th>
<th>Pfizer Inc. (USA)-BioNTech SE (Germany)</th>
<th>Moderna Inc. (USA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine Name</strong></td>
<td>COVID-19 mRNA vaccine BNT162b2</td>
<td>COVID-19 mRNA vaccine mRNA-1273</td>
</tr>
<tr>
<td><strong>Vaccine Platform</strong></td>
<td>LNP-encapsulated, non-replicating, nucleoside-modified mRNA vaccine\textsuperscript{12,13}</td>
<td>LNP-encapsulated, non-replicating, nucleoside-modified mRNA vaccine\textsuperscript{14,15}</td>
</tr>
<tr>
<td><strong>Antigenic Target</strong></td>
<td>SARS-CoV-2 spike (S) glycoprotein\textsuperscript{12,13}</td>
<td>Pre-fusion SARS-CoV-2 spike (S) glycoprotein\textsuperscript{14, 15}</td>
</tr>
<tr>
<td><strong>No. of Doses Administered</strong></td>
<td>2 doses\textsuperscript{13}</td>
<td>2 doses\textsuperscript{14, 15}</td>
</tr>
<tr>
<td><strong>Dosage</strong></td>
<td>30 µg of mRNA per 0.3 mL dose\textsuperscript{13}</td>
<td>100 µg of mRNA per 0.5 mL dose\textsuperscript{15}</td>
</tr>
<tr>
<td><strong>Adjuvant</strong></td>
<td>No\textsuperscript{12,13}</td>
<td>No\textsuperscript{14, 15}</td>
</tr>
<tr>
<td><strong>Recommended Interval</strong></td>
<td>21 days (3 weeks)\textsuperscript{13}</td>
<td>28 days (4 weeks)</td>
</tr>
<tr>
<td><strong>Route of Administration</strong></td>
<td>Intramuscular (IM)\textsuperscript{12,13}</td>
<td>Intramuscular (IM)\textsuperscript{14,15}</td>
</tr>
<tr>
<td><strong>Storage Conditions</strong></td>
<td>- 70 °C ± 10 °C for 6 months\textsuperscript{13}</td>
<td>- 20 °C ± 5 °C for 6 months \textsuperscript{16}</td>
</tr>
<tr>
<td></td>
<td>Once thawed, 2 to 8 °C for 5 days</td>
<td>Once thawed, 2 to 8 °C for up to 30 days</td>
</tr>
<tr>
<td></td>
<td>Do not refreeze</td>
<td>Do not refreeze</td>
</tr>
</tbody>
</table>
Focus On COVID-19 vaccines: mRNA vaccines

References


Citation

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