Immunogenicity and adverse events following immunization with alternate schedules of authorized COVID-19 vaccines in Canada: MOSAIC study (Mix and match of the second cOvid-19 vaccine dose for SAfety and ImmunogeniCity: a Canadian Immunization Research Network Study (CIRN)

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Introduction

In the first months of the COVID-19 vaccine rollout in Canada, 4 of 7 vaccines for which there were advanced purchase agreements were available. Worldwide demand, manufacturing processing delays, and program implementation capacity limitations meant *prioritization of limited supply at the time of a health emergency was necessary*. Recommendations were made to to increase the interval between the first two doses and permit "mix and match" across platforms. No direct evidence was available to support this was available at the time.

Objective

To evaluate reactogenicity and immunogenicity of homologous(matched) and heterologous (mixed) 1st and 2nd dose(D) of the primary COVID-19 (C19) vaccine schedule, of short and long inter-D intervals (***MOSAIC-1***), and of a mix/matched 3rd (booster) D (***MOSAIC-2***).

Methods

Multi-centre, ongoing, randomized, controlled, single-blinded clinical trial conducted in 5 provinces (BC, MAN, ON, PQ, NS) by the CIRN Clinical Trials Network (CTN) with the CIRN Reference Laboratory Network (RLN) and public health during the COVID-19 vaccine rollout *NCT04894435*

Participants randomized to one of 13 study groups based on age and prior vaccine receipt.

Safety outcomes are collected by participant report, and ***immunogenicity outcomes*** (anti-S, anti-N, anti-Receptor Binding Domain; pseudo-neutralization, and in a subset: antibody (Ab) avidity, Ab-dependent cellular cytotoxicity, T cell function and RNA seq prior to vaccine and over 12 months post vaccine.

The ***primary outcomes*** are noninferiority analysis (MOSAIC-1) or ratios of Geometric Mean Titers (MOSAIC-2) of anti-Spike titers.

Results

Launching the study:

– pace of institutional responses during a pandemic

Application for CITF funding for *MOSAIC-1* was submitted Feb 9, 2021; CITF approval occurred March 30. Health Canada (BGTD) approved the study on May 5th; PHAC approval was received on 21 May. Contract negotiation began 21 May and was executed June 28th, 2021 (almost 5 months from CITF submission), leading to subsite contract executions.

Health Canada regulatory review processes under the Interim Order were rapid; Research Ethics Board (REB) were initially timely (2020), but more prolonged later in the pandemic (2021-2022).

– readiness of the CIRN Clinical Trials Network to conduct RCTs

In place since 2009, CTN had personnel and established processes and standards of practice (SOPs) for GCP compliant study conduct, e-CRF data management and analysis. This allowed rapid preparation of protocols and procedures. A CIHR pandemic readiness grant to CIRN supported preparation for readiness to conduct Canadian COVID-19 vaccine trials

Willingness of Canadians to participate

Promotion of the study through announcements, media outlets and social media led to enthusiastic responses from potential participants; however many decided to get vaccine locally outside the study due to delay in local site opening awaiting institutional approvals, and lack of study staff during the pandemic. Some study sites could not enrol until subsite contract execution.

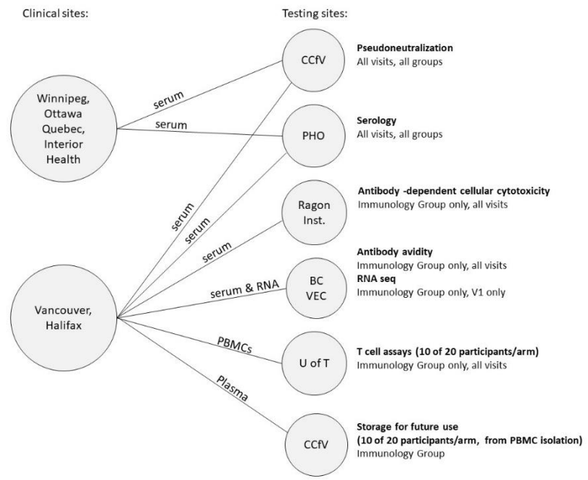
Enrolment

MOSAIC-1 The first visit for the first subject (FSFV) was 1 June 2020, the LSLV on Nov 2, 2021. (n=221)

MOSAIC-2 FSFV Dec 20, 2021, LSLVs began 2 Dec 2022, ends 13 June 2023. (n = 442)

A *Data Safety Management Board* is in place; no safety signals have been identified.

Processing of laboratory specimens is in progress at five laboratories:



Learning

Large and complex sample processing, reconciliation and shipping led by CIRN Research Laboratory Network through PHO; scanning technology introduced to some participating labs

Improved enrolment and quicker study start in MOSAIC-2 (contract in place; via new collaboration with PHAC there was easier access to provincial vaccines supplies)

Improved ability to answer public health questions (NACI Executive secretary joined CIRN Management Committee and PHAC scientist joined MOSAIC investigator team)

For further information

NCT04894435 clinicaltrials.gov

https://cirnetwork.ca/mosaic/

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