Public Health Ontario | Santé publique Ontario

SYNOPSIS

01/11/2021

Review of "Efficacy and safety of mRNA-1273 SARS-CoV-2 vaccine"

Article citation: Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2020 Dec 30 [Epub ahead of print]. Available from: https://doi.org/10.1056/NEJMoa2035389

One-minute summary

- The authors report interim findings of a phase-3 randomized, stratified, observer-blinded placebo-controlled trial to evaluate the efficacy and safety of the Moderna mRNA-1273 COVID-19 vaccine.
- The trial was conducted at 99 sites in the United States and included **adults ≥ 18 years old** with **no known history of COVID-19**, and **with locations or circumstances that put them at an appreciable risk of COVID-19 infection and/or its complications**. Participants were randomly assigned in a 1:1 ratio and stratified by age and COVID-19 complication risk criteria to receive **two doses** of intramuscular vaccine or placebo **28 days apart**.
- The **primary efficacy endpoint was prevention of symptomatic COVID-19** confirmed by RT-PCR on nasopharyngeal or nasal swab, saliva, or respiratory sample if hospitalized; occurring ≥ 14 days after the second dose of vaccine or placebo. The **secondary efficacy endpoint was prevention of severe COVID-19**.
- **Overall vaccine efficacy** against confirmed symptomatic COVID-19 after two doses was **94.1%** (95% confidence interval, 89.3%–96.8%; P<.001), with a median study follow-up time of 64 days (range 0-92 days) in 28,207 trial participants (per protocol).
- Vaccine efficacy was **consistent across racial backgrounds, sex, age groups and presence of risk factors for severe COVID-19**.
    - 18–64 years of age, not at risk for severe COVID-19 (n = 16,799): 95.9% (90.0%–98.3%)
    - 18–64 years of age, at risk for severe COVID-19 (n = 4,273): 94.4% (76.9%–98.7%)
    - ≥65 years of age (n = 7,135): 86.4% (61.4%–95.2%)
    - all age groups at risk for severe COVID-19 (n = 6,373): 90.9% (74.7%–96.7%)
    - against severe COVID-19: 100% (with all 30 cases occurring in the placebo group)
- The **incidence** of COVID-19 in the vaccine and placebo groups **began to diverge at 14 days after the first dose**.
- **Solicited local and systemic reactions were more common in vaccine recipients, than placebo recipients and more common among participants 18–64 years of age, than those ≥ 65 years of age in the 7 days following vaccination.**
    - Most local reactions (e.g., pain, erythema, swelling, lymphadenopathy) were **mild to moderate**.

    - Systemic reactions (e.g. fatigue, headache, myalgia, chills, arthralgia, nausea or vomiting, fever) occurred in 54.9% vs. 42.2% after the first dose and 79.4% vs. 36.5% after the second dose in the vaccine vs. placebo groups. The duration of the systemic adverse events after the first and second doses is 2.6 and 3.1 days (mean), respectively; reaction severity increased after the second dose.
- **Serious adverse events were rare in both vaccine and placebo groups (0.6% in both). Treatment-related severe adverse events were more common in vaccine than placebo recipients** (0.5% vs 0.2%) and independent of participants' age. There were **no treatment-related deaths reported** in any participants during the 28 days after any injection. However, the authors called for close monitoring of the slight excess of Bell's palsy that occurred in 3 participants in the vaccine group compared to 1 in the placebo group.

Additional information

- The mRNA-1273 vaccine is a **lipid-encapsulated mRNA vaccine encoding a perfusion stabilized spike protein** of SARS-CoV-2. Each dose contains **100 μg of mRNA-1273**.
- A total of 236 participants developed symptomatic COVID-19 starting 14 days after the first dose (11 in vaccine group and 225 in placebo group), corresponding to a **vaccine efficacy of 95.2% (95% CI: 91.2%–97.4%) after the first dose**. However, the trial was not designed to determine efficacy with one dose of vaccine, as 96.4% of the 30,418 randomized participants received two doses.
- Of the 28,207 participants included in the per-protocol efficacy analysis:
    - **Median follow-up time = 64 days** (range: 0–97 days) after the second dose.
    - Male: 52.6%
    - Mean age = 51.6 years (range: 18–95 years)
        - 18–64 years and not at risk for severe COVID-19: 58.1%
        - 18–64 years and at risk for severe COVID-19: 16.6%
        - ≥ 65 years: 25.3%
    - Racial or ethnic background as reported by participants:
        - white: 79.5%
        - black or African American: 9.7%
        - Asian: 4.6%
        - multiracial or other: 2.1% each
        - American Indian or Alaska Native: 0.8%
        - Native Hawaiian or other Pacific Islander: 0.2%
    - Mean body-mass index (± standard deviation): 29.3 ± 6.7
    - Risk factors for severe COVID-19 infection:
        - diabetes (type 1, type 2, gestational): 9.6%
        - body-mass index ≥ 40: 6.7%
        - significant cardiac disease (e.g., heart failure, congenital coronary artery disease, cardiomyopathies, or pulmonary hypertension): 5.0%
        - chronic lung disease (e.g., emphysema, chronic bronchitis, idiopathic pulmonary fibrosis, cystic fibrosis, or moderate-to-severe asthma): 4.8%
        - liver disease: 0.7%
        - HIV infection: 0.6%
- Severe COVID-19 was defined as the occurrence of COVID-19 as per the primary endpoint AND any of the following:

    - Clinical signs indicative of severe systemic illness, including respiratory rate ≥ 30 per minute, heart rate ≥ 125 beat per minute, oxygen saturation ≤ 93% on room air at sea level, or ratio of arterial oxygen partial pressure to fractional inspired oxygen < 300 mmHg.
    - Respiratory failure or acute respiratory distress syndrome.
    - Clinically significant acute renal, hepatic or neurologic dysfunction.
    - Admission to an intensive care unit or death.
- The authors noted the following limitations in the trial design:
    - It was not intended to evaluate the efficacy of a single dose.
    - Only the short term safety and efficacy of the vaccine was studied.
    - The data were insufficient to assess efficacy against asymptomatic infection or viral transmission.
    - The trial was conducted in the context of implemented nation-wide pandemic preventive measures such as public masking and social distancing.
    - Children, adolescents and pregnant women were excluded.
    - Efficacy evaluation in older adults, ethnic or racial minorities, and persons with prior COVID-19 was not possible due to small numbers.

PHO reviewer's comments

- Additional studies are needed to assess (1) vaccine effectiveness against infection and/or severe outcomes in vulnerable groups (e.g., persons with social deprivation); (2) vaccine efficacy and safety data in populations excluded from clinical trials (e.g., children, adolescents, pregnant and breastfeeding women, individuals with autoimmune conditions and immunosuppressed states due to disease and/or treatment); (3) duration of vaccine protection; (4) vaccine effectiveness in preventing death, hospitalization, asymptomatic infection and reducing viral transmission.
- As COVID-19 infections with onset within 14 days after the second dose were excluded, vaccine efficacy prior to two weeks after the second dose was not assessed.
- Given the limited evidence on the duration of protection and effectiveness in preventing asymptomatic infection and reducing viral transmission, all layers of public health measures for preventing COVID-19 should still be practised regardless of immunization status until further data are available.

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of "Efficacy and safety of mRNA-1273 SARS-CoV-2 vaccine". Toronto, ON: Queen's Printer for Ontario; 2021.

Disclaimer

Public Health Ontario

Public Health Ontario is an agency of the Government of Ontario dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, front-line health workers and researchers to the best scientific intelligence and knowledge from around the world.

For more information about PHO, visit publichealthontario.ca.

Ontario