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SYNOPSIS

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Review of "Safety and Efficacy of the BNT162b2 mRNA COVID-19 Vaccine"

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One-minute summary

- This is a report of the safety and efficacy findings from the phase 2/3 part of an **ongoing multinational, randomized placebo-controlled, double-blind trial of the BNT162b2 vaccine in preventing symptomatic COVID-19 in persons 16 years of age or older after two doses (30 μg each) at 21 days apart**.
- **Vaccine efficacy (95% credible interval)** at least 7 days after the second dose was reported at:
  - **95.5% (90.3% to 97.6%) in those without evidence of prior infection** (n=36,523)
  - 94.6% (89.9% to 97.3%) in those with or without evidence of prior infection (n=40,137)
- **Vaccine efficacy (95% confidence interval)** at least 7 days after the second dose among **persons with underlying conditions** (based on the Charlson Comorbidity Index) **and no evidence of prior infection** was reported at:
  - Overall (n=16,059): 95.3% (87.7% to 98.8%)
  - 16-64 years of age (n=11,795): 95.9% (87.6% to 99.2%)
  - ≥65 years of age (n=4,256): 91.7% (44.2% to 99.8%)
  - Obese (body-mass index ≥ 30.0) (n=12,103): 95.4% (86.0% to 99.1%)
  - Obese 16-64 years of age (n=9,523): 94.9% (84.4% to 99.0%)
  - Obese and ≥65 years of age (n=2,578): 100.0% (27.1% to 100.0%)
- In a **modified intention-to-treat analysis (n=43,355), vaccine efficacy** (95% confidence interval) **against COVID-19 and severe COVID-19** (see Additional information) were:
  - 52.4% (29.5% to 68.4%) and 100.0% (-51.5% to 100.0%), respectively, before dose 2
  - 90.5% (61.0% to 98.9%) and 100.0% (-3800.0% to 100.0%), respectively, at dose 2 to 7 days after
  - 94.8% (89.8% to 97.6%) and 75.0% (-152.6% to 99.5%), respectively, ≥7 days after dose 2
- **Protective effect through vaccination was observed by 12 days after the first dose** when the cumulative COVID-19 incidence among placebo and vaccine recipients began to diverge.
- **Severe systemic events were reported in <2% of vaccine recipients** after either dose except for fatigue (in 3.8%) and headache (in 2.0%) after the second dose. There were **no deaths related to the vaccine**, placebo or COVID-19.

- The authors concluded that two doses of the BNT162b2 vaccine provided 95% protection against symptomatic COVID-19 and were safe over a median of two months in persons at least 16 years of age.

Additional information

- BNT162b2, produced by BioNTech and Pfizer, is a lipid nanoparticle-formulated, nucleoside-modified RNA vaccine administered intramuscularly. The vaccine encodes a membrane-anchored SARS-CoV-2 full-length spike protein.
- Adults **eligible** for the trial were ≥16 years of age, healthy or had stable chronic medical conditions (e.g., HIV, hepatitis B, hepatitis C). This report does not include safety results for the 196 participants with HIV infection as per the protocol plan to analyze separately.
- Key criteria for **exclusion** from the trial included a previous diagnosis of COVID-19, being on immunosuppressive therapy, or having an immunocompromising condition. Also not included in this report was efficacy for pregnant and breastfeeding women.
- Out of 44,820 persons screened between July 27 and November 14, 2020 at 152 sites in six countries, 43,548 at age ≥16 years old were randomized to receive either the vaccine or a saline placebo, and 43,448 received injections.
- By October 9, 2020, **37,706 participants had a median of ≥ 2 months safety data after the second dose**:
    - 19,075 (50.6%) were male
    - median age (range) at vaccination was 52 years (16 to 91); 21,785 (57.8%) were 16–55 years of age, 15,921 (42.2%) were >55 years of age
    - 13,218 (35.1%) had body-mass index ≥30.0
    - 21% had at least one coexisting condition
    - 28,914 (76.7%) the United States; 5,764 (15.3%) were from Argentina; 2,284 (6.1%) Brazil; 774 (2.0%) South Africa
- **Vaccine efficacy** was estimated by 100 × (1 - IRR), where IRR (incidence rate ratio) is the calculated ratio of confirmed cases of COVID-19 per 1000 person-years of follow-up in the active vaccine group to the corresponding illness rate in the placebo group.
- **Primary end points** of the trial were efficacy against COVID-19 with onset ≥7 days after the second dose:
    - in persons with no serologic or virologic diagnosis up to 7 days after the second dose (n=36,523)
    - in participants with and without evidence of prior COVID-19 infection (n=40,137)
- Major **secondary end points** of the trial were efficacy against **severe COVID-19** as defined by the United States Food and Drug Administration: clinical signs at rest indicative of severe systemic illness; respiratory failure; evidence of shock; significant acute renal, hepatic or neurologic dysfunction; admission to an intensive care unit; or death.
- **Confirmed COVID-19 was defined according to the FDA criteria** which include at least one symptom and a positive nucleic acid amplification-based test result on a respiratory specimen obtained within obtained during the symptomatic period or within 4 days before or after symptom onset.
- Local reactions (pain, swelling, erythema) and systemic reactions (e.g., fatigue, headache, myalgias, joint pain, chills) were reported more often by vaccine recipients.
    - Local reactions:
        - Mostly mild to moderate in severity and tended to resolve within 2 days.

        - Pain at injection (most frequently noted) was reported less often by those >55 years of age; <1% of participants (across all ages) reported severe pain.
        - The reported frequency of occurrence did not increase after the second dose.
    - Systemic reactions (i.e., fever, fatigue, headache, chills, vomiting, diarrhea, muscle pain, joint pain, use of antipyretic medication) were more commonly reported by those 16-55 years of age and more frequently after the second dose.
- Further study is required to address:
    - Safety and efficacy beyond two months, and in pregnant women and persons younger than 16 years of age.
    - Efficacy against asymptomatic COVID-19 and transmission.
    - Management for those who missed the second dose.

PHO reviewer's comments

- While individuals with heart failure, hematological malignancy and social deprivation may be more likely to have severe disease, die or be hospitalized due to COVID-19, only 0.1% of the trial participants had leukemia, 0.1% had lymphoma, and 0.5% had congestive heart failure. Additional studies are needed to assess vaccine efficacy against infection and/or severe outcomes in these vulnerable groups, as well as in children, adolescents, pregnant women and long-term care home residents.
- Given the limited evidence on the duration of protection, effectiveness in preventing asymptomatic infection and reducing viral transmission, all layers of public health measures for preventing COVID-19 should still be practised by everyone.

Citation

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