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Inactivated SARS-CoV-2 vaccine (BBV152)-induced protection against symptomatic COVID-19

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For **Our World in Data statistics on the COVID-19 pandemic** see https://ourworldindata.org/coronavirus

For the **WHO Tracking COVID-19 variants page** see https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/

Large-scale COVID-19 vaccine campaigns are ongoing globally, with more than 7·1 billion COVID-19 vaccine doses administered; however, in the past week alone (up to Nov 1, 2021), more than 3·0 million cases have been confirmed and more than 50 500 deaths have been documented. At present, the delta (B.1.617.2) variant is outcompeting all other SARS-CoV-2 variants as the most predominant variant of concern (VOC) globally, showing substantially higher transmissibility than other VOCs.[1] Notably reduced vaccine effectiveness against the delta variant has been reported in real-world studies or case-control studies of the BNT162b2 vaccine or ChAdOx1 nCoV-19 vaccine.[2] The surge in breakthrough cases among vaccinated people highlights the extraordinary transmissibility of the delta variant. Therefore, the report in *The Lancet* by Raches Ella and colleagues is a welcome advance;[3] in a phase 3 trial of an inactivated SARS-CoV-2 vaccine (BBV152) based on an Asp614Gly variant, the authors found a substantial reduction in symptomatic COVID-19.

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The trial followed a double-blind, randomised, placebo-controlled, phase 3 design in 25 hospitals in India to evaluate the efficacy, safety, and immunological lot consistency of BBV152.[3] A total of 25 798 adult participants (aged ≥18 years) were randomly assigned, of whom 24 419 received two doses of BBV152 (n=12 221) or placebo (n=12 198). The primary outcome was a first occurrence of laboratory-confirmed (RT-PCR-positive) symptomatic COVID-19, including severe disease, with onset at least 14 days after the second dose. As a case-driven study, 130 cases of symptomatic COVID-19 were required for efficacy analysis, which occurred in 16 973 initially seronegative participants who had at least 2 weeks of follow-up after the second dose. 24 cases occurred in the vaccine group (n=8471) and 106 in the placebo group (n=8502), providing an overall estimated vaccine efficacy of 77·8% (95% CI 65·2–86·4), with efficacies of 79·4% (66·0–88·2) in participants younger than 60 years (n=15 115) and 66·2% (33·8–84·0) in older participants (≥60 years; n=1858). 16 cases of severe symptomatic COVID-19 were reported, one in the vaccine group and 15 in the placebo group, resulting in an efficacy of 93·4%

(57·1–99·8). Vaccine efficacy against asymptomatic COVID-19 infections was 63·6% (29·0–82·4). Although the 95% CIs for efficacy against asymptomatic infections are wide, the lower limit of 29·0 still indicates clinically significant protection for public health. 50 samples overall tested positive for the delta variant, 13 in the vaccine group and 37 in the placebo group, giving a vaccine efficacy against delta variant disease of 65·2% (33·1–83·0). Nevertheless, further investigations are necessary to confirm this preliminary efficacy against the delta variant and other VOCs. In a different study, the neutralisation activity induced by BBV152 against the delta variant was 2·7-times lower than that against the Asp614Gly variant.[4] In the study by Ella and colleagues, in all the delta-positive cases, the viral load in vaccine recipients was significantly lower than in placebo recipients. The concentrations of neutralising antibodies elicited by two doses of BBV152 were similar at day 56 (1 month after the second dose) in both younger and older participants or men and women. Additionally, BBV152 was well tolerated; the same proportion of participants (12·4%) reported adverse events in the vaccine group (1597 of 12 879 participants) and placebo group (1597 of 12 874), with no clinically significant differences in the distributions of solicited, unsolicited, or serious adverse events between the vaccine and placebo groups, and no cases of anaphylaxis or vaccine-related deaths. The authors concluded that the BBV152 vaccine had an acceptable safety profile, with similar safety results to other inactivated SARS-CoV-2 vaccine candidates.

This study was conducted in India, and only Indian participants were involved, making the study cohort less ethnically diverse, and limiting the generalisability of the results to other populations. Efficacy estimates for identified variants (n=79) were generated from the delta variant (n=50, 63·3%), kappa (B.1.617.1) variant (n=11, 13·9%), alpha (B.1.1.7) variant (n=4, 5·1%), and 14 other variants (n=14, 17·7%). In addition, the study provides evidence of protection against asymptomatic infection that might be of public health significance, which has not been reported in previous trials of other SARS-CoV-2 vaccines. Generally, the apparent protection against severe COVID-19 is most crucial, but the capability of preventing asymptomatic infection would also protect against mild disease, transmission, and eventually might lead to a reduction in subsequent cases of severe COVID-19.

WHO issued an emergency use listing for BBV152 on Nov 3, 2021;[5] the vaccine has already received emergency use authorisation in several countries, including India, Iran, Mexico, and the Philippines,[6-8] which are currently experiencing high SARS-CoV-2 prevalence and low to moderate vaccination coverage. The roll-out of BBV152 might ease the ultra-cold chain requirements of other SARS-CoV-2 vaccine platforms, increase the finite global manufacturing capacity, and improve insufficient supply of vaccines which disproportionately affects low-income and middle-income countries.[9]

The next step for studies of BBV152 should be a focus on monitoring for epidemiological variations in SARS-CoV-2 and the long-term vaccine efficacy against symptomatic COVID-19 and asymptomatic infection to identify whether the vaccine provides ongoing protection when any VOC replacement (other than by the VOCs investigated in this study) has occurred.

We declare no competing interests.

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