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Fourth dose of SARS-CoV-2 vaccine approved in US

Protection from symptomatic disease caused by the Omicron strain of Covid-19 wanes relatively quickly after each dose of mRNA vaccine. In a retrospective study of nearly one million people in Qatar, two doses of BNT162b2 (Pfizer & BioNTech) or mRNA-1273 (Moderna) prevented ~50% of symptomatic cases for 3 months, whereas the number rapidly decreased to ~10%. A higher level of protection was restored after the booster dose, again for around 3 months.1

The level of protection was comparable for both variants of Omicron, BA.1 and BA2, the latter now accounting for >80% of global cases. Vaccine efficacy against hospitalization did not change with time and has remained at >90%, according to the study.

The issue of waning vaccine effectiveness might have to be tackled with further doses. The US Food and Drug Administration (FDA) has granted its emergency-use authorization for the fourth dose of the mRNA vaccine for adults aged ≥50 years and for immunocompromised subjects ≥12 years of age.

In other developments, the CpG- and alum-adjuvanted peptide vaccine SCB-2019 (Clover) demonstrated nearly 100% efficacy against severe Covid-19 and hospitalizations, with no signs of waning after 5 months. The Phase 2/3 trial enrolled >26,000 subjects. The vaccine, which consists of a stable trimerized spike protein, is also being investigated as a universal booster.

The synthetic, attenuated modified vaccinia virus Ankara- vectored vaccine COH04S1 was safe and induced both humoral and cellular responses in a Phase 1 trial with young adults.2 The vaccine, which targets both the spike and capsid proteins of SARS-CoV-2, is designed to induce specific T cells, and is being investigated in immunocompromised cancer patients who cannot produce a high enough level of neutralizing antibodies.

Expanded indication for the PD-1 inhibitor pembrolizumab

The FDA has expanded approval for the immune checkpoint inhibitor pembrolizumab (Keytruda, Merck) to be used as a second-line treatment in microsatellite instability-high or mismatch repair-deficient, advanced endometrial carcinoma. The decision follows additional results from the Phase 2 KEYNOTE-158 trial showing an overall response rate of 46% in this population, with 12% complete responses, at 16 months.

Adjuvant pembrolizumab also reduced the risk of recurrence or death by 24%, compared to placebo, in patients with early-stage non-small cell lung cancer (NSCLC) enrolled into a Phase 3 KEYNOTE-091 trial. The median disease-free survival was 54 months, regardless of the level of PD-L1 expression.

Clinical development of PD-1 inhibitors on multiple fronts

The checkpoint inhibitor nivolumab (Opdivo, BMS) has been granted two approvals by the FDA. The first was in combination with the LAG-3 inhibitor relatlimab (BMS) for treatment of unresectable or metastatic melanoma. LAG-3 is another checkpoint found on the surface of T cells, which contributes to exhaustion of tumor-infiltrating subset. In the Phase 3 RELATIVITY-047 trial, the combination doubled progression-free survival time (PFS) compared to nivolumab alone.

Second, nivolumab with platinum chemotherapy was approved as neoadjuvant treatment of NSCLC. This combination reduced the risk of recurrence by almost 40% in patients with stage IB to IIIA disease enrolled in the Phase 3 CheckMate-816 trial. Subjects in the experimental arm reported a > 31-month event-free survival.

Another PD-1 inhibitor, toripalimab (Junshi Biosciences), improved overall survival of untreated advanced squamous or non-squamous NSCLC in a Phase 3 trial. The combination improved PFS to 8.4 months, compared to 5.6 months in subjects receiving chemotherapy alone. PFS at 1 year was 37% and 17%, respectively.

Finally, the PD-L1 antagonistic MAb durvalumab (Imfinzi, AstraZeneca) along with chemoradiotherapy failed to improve PFS in locally advanced cervical cancer in the Phase 3 CALLA trial. Durvalumab is used in the treatment of NSCLC and bladder cancer.

Japan reinstated HPV vaccine recommendation

Japan has recommended that all girls aged 12–16 years get the HPV vaccine, thus ending a nine-year period without such a recommendation. The decision to suspend the HPV vaccine recommendation in 2013 due to safety concerns, which were not fully borne out, led to a huge drop in coverage from 70% to less than 1%. Thousands of extra deaths from cervical cancer are expected as a result of this drop in coverage.
Late-Stage chikungunya vaccine trial meets all endpoints

A single injection of the chikungunya vaccine candidate VLA1553 (Valneva) induced protective antibody levels in 99% of >4,000 participants of the Phase 3 VLA1553–301 trial, including elderly subjects. The trial, which was conducted in the US, confirmed an acceptable safety profile, with the majority of adverse events mild or moderate.

VLA1553 previously received fast-track designations in the US and the EU, given that there is no approved chikungunya vaccine.

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References

1. Chemaitelly H, Ayoub HH, AlMukdad S, Coyle P, Tang P, Yassine HM, Al-Khatib HA, Smatti MK, Hasan MR, Al-Kanaani Z, et al. Duration of mRNA vaccine protection against SARS-CoV-2 Omicron BA.1 and BA.2 subvariants in Qatar. MedRxiv [Preprint]. 2022. doi:10.1101/2022.03.13.22272308.

2. Chiuppesi F, Zaia JA, Frankel PH, Stan R, Drake J, Williams B, Acosta AM, Francis K, Taplitz RA, Dickter JK, et al. Safety and immunogenicity of a synthetic multiantigen modified vaccinia virus Ankara-based COVID-19 vaccine (COH04S1): an open-label and randomised, phase 1 trial. Lancet Microbe. 2022;3(4):e252–e264. doi:10.1016/S2666-5247(22)00027-1.