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Fourth Covid-19 vaccine approved in US
The US Food and Drug Administration (FDA) has granted emergency-use authorization to the advan
taged protein subunit vaccine NVX-CoV2373 (Novavax) for use in adults. The decision is based on a Phase 3 clinical trial showing >90% overall efficacy against Covid-19 infection with 80% efficacy in older adults. Many countries have started vaccinating their populations with the fourth dose of an mRNA vaccine. A study of >40,000 elderly residents of long-term care facilities in Israel showed that the fourth dose of the BNT162b2 vaccine (Pfizer & BioNTech) decreases the risk of hospitalization and death due to infection with the Omicron variant by 64% and 72%, respectively, compared to the three-dose regimen alone. Vaccines are also being developed specific for emerging variants of SARS-CoV-2. The Omicron-specific booster vaccine mRNA-1273.214 (Moderna) elicited 1.7-fold higher levels of neutralizing antibodies, compared to the parental booster vaccine mRNA-1273. These antibodies were specific for strains BA.4 and BA.5 currently in circulation. Mucosal immunity was stimulated by the oral tablet vaccine VXA-CoV2–1 (Vaxart) in a Phase 1 trial involving 35 healthy adults. The vaccine, which comprises a non-replicating adenoviral vector expressing the spike and nucleocapsid antigens with a double-stranded RNA adjuvant, elicited IgA antibodies reactive against multiple coronaviruses and persistent for at least one year.

IL-2 immunotherapy was beneficial for solid-cancer patients
A 40% tumor-control rate was achieved in ten evaluable patients who received the IL-2 superagonist MDNA11 (Medicenna). This part of the dose-escalation Phase 1/2 ABILITY trial enrolled 14 subjects with advanced solid cancers who had failed at least four prior lines of therapy. MDNA11 is designed to stimulate intratumoral CD8+ and NK cells.

Clinical development of norovirus vaccines
The bivalent VLP norovirus vaccine HIL-214 (HilleVax) elicited antibodies that persisted at least five years after vaccination. The Phase 2 NOR-213 trial involved >500 adults who had received one or two doses of the vaccine adjuvanted with alum and monophosphoryl lipid A. Antibody levels at the 5-year mark were comparable to those at an earlier follow-up.

Another candidate, the oral norovirus vaccine VXA-GI.1 NN (Vaxart), was safe and induced dose-dependent levels of IgA-secreting cells in healthy adults 55–80 years old, enrolled in the dose-escalation, placebo-controlled Phase 1b trial. The vaccine, which is administered in two doses, consists of an adenovirus vector expressing the major capsid protein of norovirus GI.1.

New checkpoint inhibitor extends survival in esophageal cancer
First-line treatment with the combination of the PD-1 inhibitor tisilizumab (Novartis & BeiGene) and chemotherapy extended overall survival by >6 months compared to chemotherapy alone in patients with unresectable, advanced or metastatic esophageal squamous cell carcinoma. The randomized Phase 3 RATIONALE 306 trial, which enrolled 650 patients, reported objective response rate of 63% and 42% in the experimental and control groups, respectively, regardless of PD-L1 blood levels. Esophageal cancer has a poor prognosis with a 5% five-year survival rate.

EU approves smallpox vaccine for prevention of monkeypox
The European Commission extended the authorization of the smallpox vaccine MVA-BN (Imvanex, Bavarian Nordic) to include protection from monkeypox. The vaccine, which had already been used by several countries in an off-label regimen, consists of a non-replicating modified vaccinia Ankara virus.

The current epidemic of monkeypox involves outbreaks in 75 countries where the virus is not endemic. The infection spreads through close contact and body fluids.

Personalized cancer vaccine passes first test in pancreatic cancer
The personalized neoantigen mRNA vaccine autogene cveu
eran (BioNTech) in combination with the PD-1 inhibitor atezolizumab (Roche) and chemotherapy demonstrated safety and signs of clinical activity in subjects with resected pancreatic ductal adenocarcinoma. Half of 16 patients reported neoanti
gen-specific T-cell formation and longer recurrence-free survival. Autogene cveu raneran is a lipid-delivered mRNA vaccine encoding up to 20 neoantigens derived from bioinformatical analysis of deep-sequenced tumors obtained from each patient.
Pneumococcal vaccine approved for children

The FDA has approved the 15-valent pneumococcal conjugate vaccine Vaxneuvance (Merck) for children aged 6 weeks to 17 years. The vaccine protects from two more strains than the currently used pediatric vaccine Prevnar 13.

The decision is based on seven clinical trials showing non-inferior immunogenicity of Vaxneuvance, compared to Prevnar 13, to the 13 shared pneumococcal strains.

Checkpoint inhibitor atezolizumab fails to improve renal-cell carcinoma

The PD-L1 inhibitor atezolizumab (Tecentriq, Roche) has failed to prevent recurrence or death in patients with renal-cell carcinoma at high risk of developing metastasis following surgery. The immunotherapeutic was tested in adjuvant setting in the Phase 3 IMmotion010 trial.

References

1. Muhsen K, Maimon N, Mizrahi AY, Boltyansky B, Bodenheimer O, Diamant ZH, Gaon L, Cohen D, Dagan R. Association of receipt of the fourth BNT162b2 dose with omicron infection and COVID-19 hospitalizations among residents of long-term care facilities. JAMA Intern Med. 2022;182(8):859–867. doi:10.1001/jamainternmed.2022.2658.

2. Johnson S, Martinez CI, Jegede CB, Gutierrez S, Cortese M, Martinez CJ, Garg SJ, Peinovich N, Dora EG, Tucker SN. SARS-CoV-2 oral tablet vaccination induces neutralizing mucosal IgA in a phase 1 open label trial. MedRxiv [preprint]. 2022. doi:10.1101/2022.07.16.22277601.

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